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# PROGRESSIVE MEDICINE

A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES  
AND IMPROVEMENTS

IN THE  
MEDICAL AND SURGICAL SCIENCES

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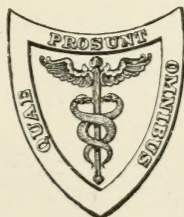
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VOLUME IV. DECEMBER, 1920

DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS, THE LIVER, PANCREAS  
AND PERITONEUM—DISEASES OF THE KIDNEYS—GENITO-URINARY DISEASES  
—SURGERY OF THE EXTREMITIES, SHOCK, ANESTHESIA, INFECTIONS,  
FRACTURES, DISLOCATIONS AND TUMORS—PRACTICAL  
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# PROGRESSIVE MEDICINE.

DECEMBER, 1920.

## DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS, THE LIVER, PANCREAS AND PERITONEUM.

By EDWARD H. GOODMAN, M.D.

**Cardiospasm.** Until 1908, cardiospasm, which is defined by Verbrycke<sup>1</sup> as an abnormal spasmodic contraction of the lower esophagus, was a comparatively rare disease (well under 200 cases having been reported). In that year, Plummer reported 40 cases coming under his personal observation, and this year (1920), Verbrycke publishes an analysis of 100 cases.

The cause of the spasm remains to be discovered, but it must undoubtedly have its origin in the nervous system. The vagus supplies both the esophagus and the cardiac sphincter, but its action on each is different. Stimulation of the vagus causes increased peristalsis of the esophagus, but the sphincter is relaxed, probably through sympathetic fibers running in the vagus; section of the vagus causes marked contraction of the cardia. It would appear that a weakened function of the vagus would account for the symptom-complex of cardiospasm. Clinically, however, Verbrycke finds this not to be the case, for in 21 cases there was just the opposite condition—vagotonia. Although not certain of the actual cause of the spasm, there are predisposing factors which operate in many cases.

*Sex* does not seem to be important as there were 39 males and 61 females in the series.

*Age.* The disease is one of middle age, over 50 per cent. appearing between the age of thirty and fifty, 20 were in the third decade, 28 in the fourth, 35 in the fifth, 12 in the sixth, and 15 between sixty and eighty.

*As types of causes,* Verbrycke finds 4: (1) Neurotic, mental and psychic; (2) reflex, (3) irritative, (4) toxic.

*Reflex causes* include appendiceal disease, gall-bladder trouble, gastric ulcer, adhesions, cancer, tonsillitis (chronic) and pylorospasm.

*Irritative Causes.* These account for the smallest number of cases and include fissure or ulcer of the cardia, diverticulum, hard pieces of food, cold drinks.

<sup>1</sup> Southern Medical Journal, 1920, xiii, 236.



*Toxic Causes.* Verbrycke believes that 28 of his cases had symptoms and signs of intestinal auto-intoxication, which signs and symptoms, I personally, regret are not disclosed by the author. Four dated their trouble from influenza and four had hyperthyroidism.

*Course of the Disease.* The average duration was two years and two months, the extremes being several weeks to forty years. Verbrycke distinguishes three stages: (1) Transient or slight obstruction; (2) decided obstruction but not dilatation; (3) dilatation of the esophagus above the spasm. There were 47 first stage, 35 second stage, and 18 third-stage cases. It is needless to emphasize that the stages naturally overlap and the gradation is not marked.

*SYMPTOMATOLOGY. Dysphagia.* This is the commonest symptom. Some patients had pain while eating and some soon after; in some, the pain persisted until regurgitation occurred, in others it wore off gradually, and in one it was continuous, which is unusual. In a few instances, the pain was like that of angina. The stage of the disease bears little relation to the pain.

*Sticking of food* is another common symptom and, like pain, it is not necessarily dependent upon the stage of the disease.

*Regurgitation and Vomiting.* Twenty-seven did not regurgitate, 23 did occasionally, 40 more markedly, 3 brought up liquids only, 3 forced food up, and 1 coughed food back. There are two types of vomiting; in the one, food comes up shortly after swallowing, this being due to cardiospasm, in the other, the patients will retain nourishment for some hours and will then vomit, this being due to pylorospasm.

Most cases of cardiospasm show a great deal of mucus in the regurgitated material. The food may be as swallowed or may be admixed with gastric juice which has regurgitated into the esophagus from the stomach. More often solid food sticks at the cardia and regurgitates, but occasionally thin liquids only will come up. This is very suggestive of cardiospasm.

*Belching*, because of its frequency in all digestive troubles, is relatively unimportant. Some loss of weight is a usual thing.

*OBJECTIVE SIGNS. 1. Swallowing Sounds.* With the stethoscope placed just below the xyphoid, the sound is heard as the cardia relaxes and a portion of water drops into the stomach. Normally, it is heard eight seconds after the patient swallows. In Verbrycke's 100 cases, the test was tried 66 times, and it was normal in only 14.

*2. Obstruction to the Stomach Tube.* In only 10 of the 96 cases in which it was tried did the tube enter the stomach freely. Several times it entered the cardia but was so firmly grasped as to cause it to stretch on withdrawal. In 2, the tube caused considerable pain, and in 2, blood was brought away. The obstruction to the stomach tube is absolutely the best diagnostic sign for first-stage and some second-stage spasms, and the author bars not even the x-ray, which he says misses some cases.

*X-ray.* Although the fluoroscope is indispensable in the diagnosis it fails, in a fair proportion of the cases, to reveal the spasm, due probably to an intermittent spasm, and secondly because the esophagus is not properly studied.

**PROGNOSIS.** With proper treatment any stage is speedily curable.

**TREATMENT** is medical, mechanical and surgical. Removal of the cause is, of course, the first thing to be done, following which spasm usually ceases. All irritating food should be avoided and general measures for building up the health should be instituted. Mineral oil before meals, to lubricate the passage, is useful. Belladonna pushed to the physiologic limit is valuable in general vagotonic cases, but is disappointing in so-called idiopathic cardiospasm.

*Mechanical treatment*, which consists in forcibly overstretching the spastic muscle, is indicated in practically all severe cases. Passage of a stiff tube, and the use of bougies are ineffectual. The author disapproves of the Einhorn instrument, preferring the Plummer water-pressure dilator. The amount of pressure employed is from 6 to 30 pounds. No matter what the pressure is if there is pain, it should be immediately lowered.

*Surgical treatment* consists of gastrostomy and is indicated only in moribund patients.

*Apropos* of an article by Aaronson,<sup>2</sup> which is along conventional lines, I must call attention to the sentence, "Drugs are absolutely worthless." With this statement I am not in accord, for I recall distinctly, during the last twelve months, a patient in a ward of the Presbyterian Hospital who was completely cured of his offending spasm, by the administration of bromids, large doses of belladonna and a bland, non-irritating semi-fluid diet. I have used belladonna frequently in such cases, and place upon it the greatest reliance, provided the spasm is a spasm of functional nature and not due to an underlying organic condition.

## DISEASES OF THE STOMACH.

**Food Factors in Gastro-enterology.** Dietetics is admitted by Mendel<sup>3</sup> to be far from being an exact science. Some of our views concerning nutrition have undergone changes as the result of the restrictions placed upon us during the war. We have learned the possibility of using more than one cereal to advantage; we have succeeded in lowering the consumption of meat without apparent detriment; we have reduced the intake of sugar to the plane where it represents a condiment rather than a food, and we have appreciated the worth of vegetables which heretofore we have regarded with some contempt. All these war-time changes have gone on without any appreciable alteration of the well-being of our organism. It must be stated that the restrictions recommended by our Food Administration caused not a little anxiety to the officials, lest the health of the people might suffer. Elsewhere, in the Central Empires of Europe, there have been numerous cases of various gastro-intestinal disorders provoked by the indigestible carbohydrates. Mendel recognizing the humoral path of stimulation through the intermediation of chemical substances—hormones or succagogues—suggests that were the various chemical secretory stimulants occurring in foodstuffs better

<sup>2</sup> New York Medical Journal, April 10, 1920, p. 624.

<sup>3</sup> American Journal of the Medical Sciences, 1919, clviii, 297.



known, diet might accomplish for secretion what we are calling upon drugs to do.

VITAMINES. Scarcely five years old,\* this word "vitamine" has become one to conjure with, and the more we know of "the hitherto unidentified food factors indispensable to normal nutrition," the less mystery will attend the employment of this term. Even if there is mystery, there is also truth, as witness, "An animal is placed upon a diet of isolated proteins, carbohydrates, fats and inorganic salts—the traditional mixture of nutrients which the physiology of our teachers has led us to expect to be adequate for the body's needs. Nutritive failure and decline will inevitably ensue, attended by a variety of symptoms, perhaps including those seen in beri-beri. An exceedingly small dose of brewer's yeast, or a chemical fraction prepared therefrom, or a small allowance of a vegetable like the tomato, spinach or carrot, or an addition of milk or any of a large variety of naturally occurring foods to the dietary, will bring a restitution of health with a speed and completeness that is little short of marvelous." This illustration of Mendel's is accompanied by others none the less poignant, serving to remind us that, in the present state of our knowledge, the gastro-enterologist cannot afford to overlook the possible role of the vitamins in the functions of those parts of the organism with which he is most directly concerned.

PROTEIN FACTORS. Not all proteins are alike in digestibility, thus the proteins of some legumes are conspicuously more resistant to digestion than are proteins from many animal and vegetable sources. Native egg white is poorly utilized, and Bateman, working in Mendel's laboratory, states "A substance which fails to stimulate a flow of gastric juice and is antipeptic, which hurries from the stomach, calls forth no flow of bile and strongly resists the action of trypsin, which is poorly utilized and may cause diarrhea, has evidently little to recommend it as a food-stuff of preference for the sound person, let alone for the invalid. And when the native protein needs only to be coagulated at 70° in order to obviate almost all the effects mentioned, there appears still less reason for using it uncooked." Bran is another food of negative digestibility. The problem of dietotherapy is not one of calories and digestible nutrients, it is a question of appropriate qualitative and quantitative mixture.

THE INORGANIC ELEMENTS. There is a question of the necessity for these substances in the diet, apart from the very obvious one of using them for structural purposes. The gastro-enterologist is particularly interested in the role of chlorin in the human economy, because of the indispensability of this element in the elaboration of gastric juice. When the intake of chlorine is restricted, the output decreases, in starvation it is almost *nil*, and whatever chlorin is secreted into the stomach is subsequently reabsorbed and consequently conserved.

FOOD AND THE INTESTINAL FLORA. It must be remembered that the intestinal flora is by no means a constant one, there being a dependence of bacterial type upon the chemical character of the diet—carbohydrates favoring the preponderance of the acid-forming types, while proteins encourage the putrefying bacteria.



McCarrison<sup>4</sup> describes changes wrought upon the intestines of pigeons by creating in their diet a deficiency of accessory food factors. These changes were essentially atrophy and congestion, leading to (1) impairment of the neuromuscular control of the bowel; impaired transport of the intestinal contents along the alimentary canal. (2) Impairment of assimilative power. (3) Impairment of secretory function. (4) Impaired protective resources leading to infection of the mucous membrane of the bowel by pathogenic saprophytes, or ingested bacteria, and to systemic infection therefrom.

He is conservative in the expression of the opinion, "Unwilling as I am to apply too directly to the human subject the experimental results of intensive "vitaminic" starvation observed in birds, we may, I think, regard the changes I have described as applicable in some degree to man." Complete "vitaminic" deprivation is rare, but incomplete deprivation or subminimal supply is frequent, and food deficiency leads directly and indirectly to intestinal changes, and McCarrison believes that it favors bacterial growth, and plays a role in such gastro-intestinal disorders as mucous disease, celiac disease and intestinal stasis.

*Mucous Disease.* This is a very common disease among European children in India who are fed largely on sterilized milk poor in vitamins, artificial foods, white bread, polished rice, poor butter, overcooked vegetables and excessive quantities of sugar. Therapeutic experience shows how rapidly it yields to limitation of carbohydrates and to a rationally balanced dietary of good "vitaminic" quality. In pigeons, a condition paralleling these human cases is found.

*Celiac Disease.* The author refers to Still's<sup>5</sup> lecture on Celiac Disease, which, on looking over previous numbers of PROGRESSIVE MEDICINE, the section of PROGRESSIVE MEDICINE devoted to Children's Diseases, I find has not been reviewed. McCarrison believes that the condition described by Still may be a deficiency disease. "Its absence in breast-fed children, its onset between the age of nine months and two years, the diarrhea which so frequently precedes it, the cessation of growth, the ill-formed, pale, 'oatmeal' stools, the frequent association of scorbutic symptoms, the abdominal distention, the afebrile nature of the malady, the diminished size of the liver, the blood changes, the occurrence of edema, the thin bones, the muscular feebleness—all these find their counterpart in pigeons fed on an exclusive dietary of autoclaved rice." McCarrison, in his birds, finds certain adrenal changes (enlargement) in "vitaminic" deprivation and suggests these may be found in man, and makes the recommendation that they be looked for in food deficiency diseases.

*Chronic Intestinal Stasis.* Keith is quoted as describing two anatomical factors in the causation of stasis: (1) Defective action on the part of the abdominal musculature. (2) Lesion of the neuromuscular system of the intestine.<sup>6</sup> McCarrison corroborates this belief and describes histopathologic changes (atrophy of all muscular tissue and neuromuscu-

<sup>4</sup> British Medical Journal, July 12, 1919, p. 36.

<sup>5</sup> Lancet, August 10, 17, 14, 1918.

<sup>6</sup> PROGRESSIVE MEDICINE, December, 1916, p. 1010.

lar lesions) which suggest to him that stasis may have a deficiency basis. Keith's pathological changes in the large bowel in stasis are strikingly similar to those found in pigeons after being fed on a "vitamine"-free food, except that McCarrison's are acute while Keith's are chronic.

In another paper, McCarrison<sup>7</sup> describes intestinal changes in monkeys on a deficiency diet. The experiments are given in great detail, with adequate pathologic reports. The sum total of pathologic changes was atrophy, congestion, dilatation and inflammation, all evidence of great malnutrition. The clinical manifestations of these changes are numerous. "There will be impaired production of digestive ferments and other secretions of the entire gastro-intestinal tract, leading to imperfect digestion, excessive carbohydrate fermentation, and distention of the stomach and intestines with gas. Depressed functional activity of the pancreas will result from the impaired production of hydrochloric acid by the pyloric glands, and of prosecretion (prosecretin?) by the duodenal glands. Impairment of the neuromuscular control of the entire tract will lead to delayed transit of the intestinal contents, especially in the colon, and weakening of its walls and "ballooning." The deranged neuromuscular control of the bowel may favor production of intussusceptions. The conditions enumerated will lead to intense toxic absorption from the intestinal tract, and impairment of the protective resources of the entire gastro-intestinal mucosa against infecting agents, leading to infection of the mucous membrane by pathogenic saprophytes and by ingested pathogenic organisms. These infections give rise to gastro-intestinal catarrh, to gastritis, duodenitis, enteritis, and colitis, and frequently to hemic infections. The occurrence of dysentery in these circumstances is significant.

1. Dietaries which are deficient in vitamins and in protein, and at the same time excessively rich in starch or in fat, or in both, are potent sources of disease, and especially of gastro-intestinal disease.

2. An excess of fat, in association with deficiency of "B-vitamine" and protein and superabundance of starch, is peculiarly harmful to the organism.

3. Certain dietetic deficiencies greatly favor the invasion of the blood and tissues by bacteria; especially is this the case when deficiency of vitamins and protein is associated with an excessive intake of starch.

4. Since life cannot be sustained in the monkey, *Macacus sinicus*, for much longer than one hundred days on a dietary almost wholly devoid of "B-vitamine," it would appear that complete absence of this vitamine from the food is of less practical importance from the point of view of the production of disease in human beings than its subminimal supply. Complete deprivation of "B-vitamine," especially if there be also imperfect balance in other essential requisites of the food, will lead to rapid dissolution and death; subminimal supply of this vitamine will lead in like circumstances, to slow dissolution and disease.

5. The results recorded in this paper may afford some explanation of the genesis of that great mass of ill-defined gastro-intestinal disorder

<sup>7</sup> British Medical Journal, February 21, 1920, p. 249.



and vague ill health which forms so high a proportion of human ailments at the present day."

In a third paper, McCarrison<sup>8</sup> summarizes the material published in the foregoing two articles, but in addition succinctly states the facts concerning our present knowledge of vitamins, a name which he considers unsatisfactory, and for which the term "advitant" has been proposed by Professor Armstrong. Vitamins are not foods in the sense of tissue builders or energy producers: they simply aid the body to utilize food material sufficiently and its cells to perform their functions. Although their true nature is unknown, they are probably of the nature of

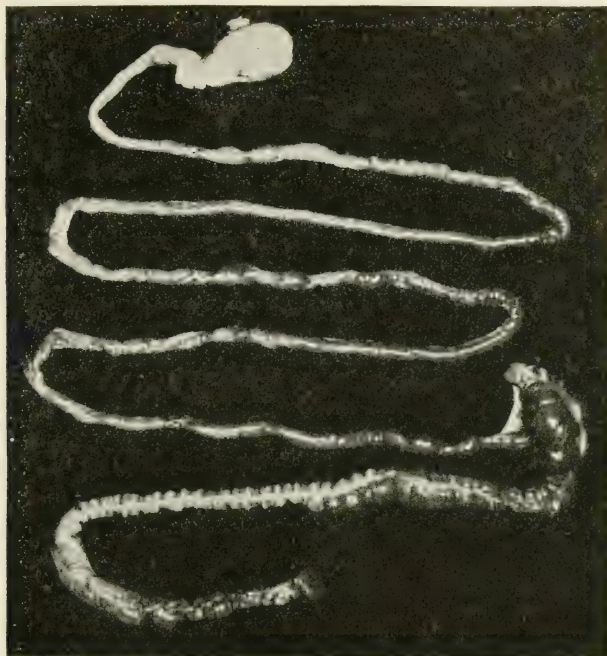


FIG. 1.—Gastro-intestinal tract of healthy adult monkey. Note size of empty stomach, normal appearance of small intestine, and the longitudinal muscular bands and rugæ of the colon.

organized catalysts or enzymes. They are found in the germs and peripheral layers of such seeds as wheat and rice, and throughout the whole seed in peas, beans and other pulses. They occur abundantly in the cells of yeast, the yolks of eggs, and in varying proportions in the different parts of plants and in the tissues and organs of the animal body. They are more plentiful in the brain, liver and kidney, than in the muscles and the animals derive them from the plants they eat. or from fresh animal foods. The animal body does not manufacture them.

Some vitamins or advitants are soluble in oils and fat and are there-

<sup>8</sup> British Medical Journal, June 19, 1920, p. 822.



fore contained in the majority of animal fats, lard, however, being said to be an exception. These fat soluble, or A-vitamines readily undergo

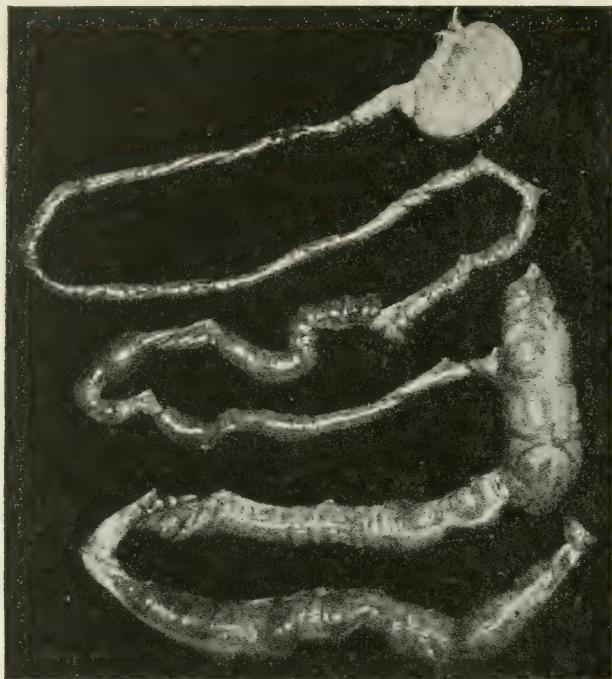


FIG. 2.—Gastro-intestinal tract of adult monkey fed on autoclaved food for ninety-eight days. Note dilatation of empty stomach, large ileal intussusception, great dilatation of colon and atrophy of its longitudinal muscular bands; also inert appearance of the colon.

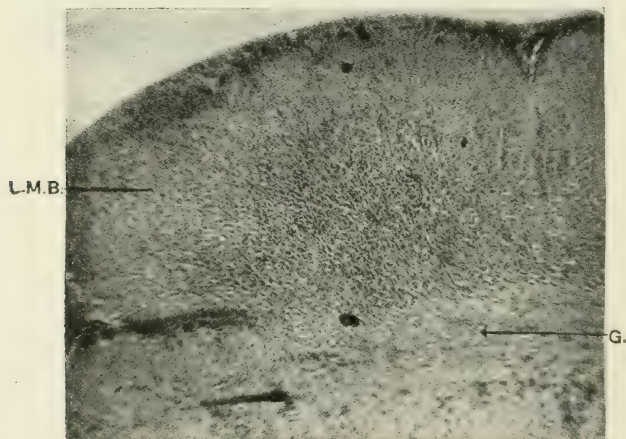


FIG. 3.—Section of wall of colon from healthy adult monkey, showing longitudinal muscular bands (L.M.B.); also ganglion of Auerbach, indicated by arrow (G).

decomposition, and they exist but sparingly if at all in vegetable oils, consequently artificial substitutes for butter do not contain them. In the green leaves and growing parts of plants they are found in abundance, but are deficient in roots and root vegetables. Butter made from



FIG. 4.—Section of wall of colon from adult monkey fed on devitaminized food. Note great atrophy of longitudinal muscular band (*L.M.B.*) and swelling and degeneration of the ganglia of Auerbach (*G*). Same magnification as Fig. 3.

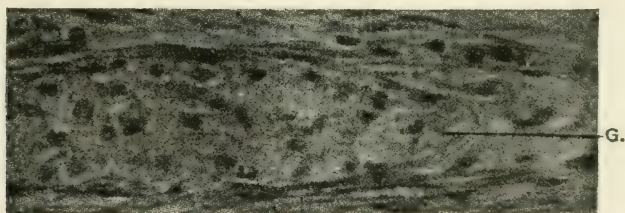


FIG. 5.—Section of ganglion of Auerbach from healthy adult monkey.  $\times 265$ .

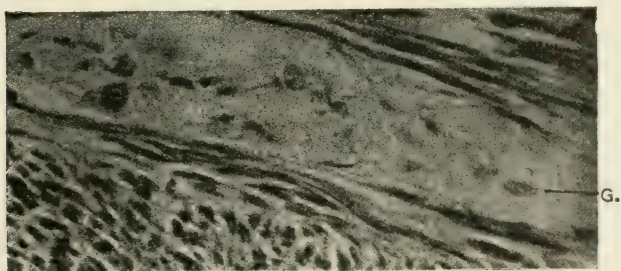


FIG. 6.—Section of ganglion of Auerbach from adult monkey fed on devitaminized food. Note swelling and degeneration of its cells.  $\times 265$ .

the milk of cows fed on green fodder contains a substance which prevents edema in pigeons, while that made from the milk of cows fed on dry fodder does not do so. McCarrison states there is reason to believe that the absence of these A-vitamines from the dietary is the actual or pre-



disposing cause of rickets. Other vitamins are soluble in water, B-vitamins, and the chief sources of these are grain, fruit and egg yolk. As they are soluble in water they are liable to be dissolved out of grains and fruit upon boiling and since they are concentrated in the germs of seeds they are frequently removed in the milling process. They are not destroyed by boiling for a short time, but exposure to temperature up to 130° C for an hour and a half destroys them. They are commonly referred to as the "antineuritic vitamins," since their absence from the food is the actual or predisposing cause of beriberi.

The third group—C-vitamins, or the "antiscorbutic"—are also soluble in water; they are found in the green parts of plants and vegetables and in fruit. They are unstable and are very susceptible to the action of heat and alkalis. They are thus very readily destroyed in the process of cooking, especially, as often happens, when sodium bicarbonate is added to the water in which vegetables are cooked. Dry grain does not contain them, they develop when the seeds germinate. Tinned or dried vegetables and fruit may contain them, but in reduced quantity and quality and not in such perfection as the fresh raw products. Experiment shows that among the food materials, lemon juice and cabbage juice are richest in them; fresh milk contains them in small amount only.

"It is seen, therefore, that though vitamins are plentifully distributed in the raw materials which both man and animals instinctively use as foods, they are very prone to be dangerously reduced in amount in their preparation for consumption. Thus, boiled polished rice, which forms the staple food of so many Eastern peoples, is often wholly devoid of them; so, too, is white flour, the staple food of so many in England."

McCarrison follows this brief résumé of the vitaminic question by a full discussion of the changes seen in the laboratory, and the changes seen in man under conditions which cause a deficient intake of vitamins. The accompanying photographs illustrate some of the gross and microscopical changes taking place in monkeys after being fed food sterilized as far as vitamins are concerned.

**Effect of Glandular Extracts on Gastric Secretion.**<sup>9</sup> 1. *Thyroid*. In Graves's disease, normal acidity as well as hyperacidity is found, and but rarely hypoacid values. In myxedema, however, there is always an acidity. When thyroid extract was given subcutaneously, acidity was always raised and digestion was carried more nearly to completion than in the controls and Boenheim suggests the use of the thyroid gland in cases of lowered acidity.

2. *Pancreas*. There is with pancreas as with thyroid gland a resulting increase in acidity and particularly is this seen in cases of achylia gastrica.

3. *Thymus*. The results with this were confusing. The acidity seemed to be increased, and digestion of protein seemed to be carried to a further stage than before. The above statement applies only to a Plasmon-meal, since with the ordinary test meal, conflicting results were obtained, sometimes acidity in hypoacidity was raised and sometimes it

<sup>9</sup> Boenheim: Arch. f. Verd. Kr., 1920, xxvi, 74.



was unaffected. When there was hyperacidity, however, the acid value was always increased.

4. *Adrenalin*. The effect of adrenalin on the gastric secretion is to lower the acidity except in cases of hypoacidity, when higher values are found after its use.

5. *Hypophysis*. There is a diminution of acidity in hyperacid cases, and in others the acidity is increased.

6. *Ovaries*. Increase of the amount of secretion and increase of acidity (Plasmon-meal) with the customary test-meal, the amount of material extracted increases but the acidity is lowered.

**Gastro-intestinal Symptoms in Thyroid Disease.** Fifty-six cases of exophthalmic goiter, 12 cases of hyperthyroidism and 43 remaining cases were analyzed by Kohn<sup>10</sup> with the following tabulated result:

	Exophthalmic goiter.	Hyper- thyroidism.	Other cases.
Past gastro-intestinal history (positive)	38	4	19
Past gastro-intestinal history (negative)	18	8	24
Present gastro-intestinal history (positive)	39	5	17
Present gastro-intestinal history (negative)	17	7	26
Disturbed appetite	19	0	3
Eruclatations	9	0	4
Nausea	15	3	7
Vomiting	20	3	8
Epigastric discomfort	15	1	6
Abdominal discomfort	8	0	9
Localized right iliac discomfort	4	1	0
Jaundice	5	0	6
Constipation	21	6	10
Diarrhea	18	2	4
Headaches	2	0	1
Splanchnoptosis	2	0	2
Hemorrhoids	3	0	5
Pulse below 85	3	2	12
Pulse above 85	11	0	12
Pulse above 100	34	7	4

Of the 111 cases, past history of gastro-intestinal disturbance occurred in 61 instances and a present history of gastro-intestinal disturbance occurred in the same number of patients. The author infers from this that gastro-intestinal manifestations are a common accompaniment of thyroid disease, and in his opinion "it is very probable that gastro-intestinal symptoms will quite often precede in assertion, let alone follow the more definite significations of thyroid disease."

Hernando<sup>11</sup> here concludes his study of this subject, read at the inaugural meeting of the Spanish Association for the Advancement of Science. He remarks that the glands with an internal secretion influence the digestive apparatus not only by their secretions but through the intermediation of the vegetative nervous system. Universal asthenia or splanchnoptosis is probably a consequence of congenital changes of this origin. Gastric secretion may be modified by the functioning of

<sup>10</sup> New York Med. Jour., December 27, 1919, p. 1066.

<sup>11</sup> Abstract, Journal of the American Medical Association, 1919, lxxiii, 1902.

the endocrine glands, but this is usually in the line of hyposecretion, although occasionally cases of hyperchlorhydria are encountered in persons with excessive thyroid functioning (the extract of the normal thyroid has a stimulating action on gastric secretion) and in persons with suprarenal insufficiency (suprarenal extract has an inhibiting action on gastric secretion). His own and others' research has demonstrated that suprarenal insufficiency seems to provide conditions favorable for the development of gastric ulcer, including the status lymphaticus, the modified functioning of the vegetative nervous system, the persistence of or increase in the hydrochloric acid in the stomach, and the low resisting powers to infection in general. He has observed gastric ulcer only in cases with symptoms of extreme suprarenal insufficiency, but probably comparatively mild insufficiency might reinforce other factors in the pathogenesis of gastric ulcer in certain cases. The injurious effect of fatigue and emotions on persons with hyperchlorhydria and gastric ulcer may be explained by the exhaustion of the suprarenals which they induce. This explains likewise the benefit realized as the suprarenals recuperate under repose, or suprarenal extract is given. He gives in conclusion 104 bibliographic references with the full titles.

**Gastric Contents.** Baufle<sup>12</sup> calls attention to a common inexactitude in all methods, namely that the terms "test-meal" and gastric juice are used synonymously. The liquid obtained by filtration after a test-meal is not pure gastric juice but a mixture, in variable proportions, of the two. Supposing that there are equal amounts of the two, then one would simply have to double his figures to obtain the real figure for acidity; if, on the contrary, there is only a small quantity of the meal remaining, the actual gastric acidity will be three or four times greater than obtained on titration. He suggests that one introduce into the meal a substance not modified by gastric secretion and not absorbed by the mucosa—the titer of this substance will then allow one to estimate what fraction of the meal is remaining at the time of extraction. In the formula

$$\frac{P}{M} = \frac{P}{R}$$

P = substance introduced; M = volume of meal; p = substance contained in the chyme at time of extraction; R = fraction of meal not evacuated. Therefore, knowing the quantity of gastric contents, C; the portion not evacuated, R; one easily obtains the quantity of gastric juice, S; thus,  $S = C - R$ .

Two substances may be introduced into the meal, phosphate of soda and iron sulphate, and Baufle prefers the latter. Calculation of this, which in the chyme, (C), belongs to the remaining meal (R), and the secreted juice S gives the co-efficient of secretion  $\frac{S}{R}$ .

The following example serves to illustrate the method. A subject receives an Ewald meal totaling 340 c.c. The total volume of recovered

<sup>12</sup> Paris médical, 1919, ix, 428.

juice (extraction and lavage of residue following Mathieu's method) is 270 c.c.; the amount of iron in the gastric contents shows that there is 90 c.c. of remaining meal and 180 c.c. of juice secreted. The amount of acidity obtained by Töpfer's method is

Free HCl . . . . .	0.584
Acid of fermentation . . . . .	0.146
Combined acid . . . . .	0.438
	<hr/>
	1.168

or in 1000 c.c. of mixture (in the proportion of 90 per cent. of meal to 180 of juice) there is an acidity of 1.168. If 180 c.c. is equal to 270 c.c.

of chyme, 1 c.c. of pure juice =  $\frac{270}{180}$ , 1000 c.c. =  $\frac{270}{180} \times 1000 = 1500$  c.c.

Hence, 1500 c.c. = volume of gastric chyme whose acidity corresponds to 1000 c.c. of chyme (from Töpfer's method) the acidity of 1500 c.c. (corresponding to 1000 c.c. pure juice) can be determined by multiplying the initial figure by 1.5, and the result is equivalent to the acidity expressed in terms of 1000 c.c. juice. In other words, let A represent acidity of a mixture C, containing S of gastric juice, the acidity of B will be determined by the formula  $A \times \frac{C}{S}$ . As a rule, to determine the acidity

of pure gastric juice independently of the meal, it is necessary simply to multiply Töpfer's figures by the co-efficient  $\frac{C}{S}$  where C represents the total volume of chyme extracted and S the juice remaining in the stomach at the same time. In the example given above:

Free acid . . . . .	0.584	$\times 1.5$	= 0.876
Combined acid . . . . .	0.438	$\times 1.5$	= 0.657
Total acid . . . . .	1.168	$\times 1.5$	= 1.752

**Sham Test-meal.** Dupuy<sup>13</sup> attempts to separate the two types of secretion, studied in animals by Pawlow, the psychic secretion, and chemical secretion; the first being the juice secreted under the stimulus of seeing, smelling, and tasting the food, and the second being the secretion aroused through actual entrance of the food into the stomach.

**Technic.** The patient presents himself in the morning, fasting, and a tube is passed to be sure that there is no stasis; if there is, lavage is practised. He is then given a piece of boiled beef, buttered bread and a glass of water; the food is to be cut, and thoroughly masticated, but nothing is to be swallowed (*en rejetant au fur et à mesure de la mastication*) the saliva and food being deposited in a vessel. Several times during the meal he should rinse his mouth with water. The meal should take about ten minutes in order to be thoroughly masticated; he then rests for ten minutes, swallowing no saliva. The tube is then passed again and about 30 to 90 c.c. of water clear fluid is recovered. Using Einhorn's duodenal tube, it will be seen that the "appetite juice" (*suc d'appetit, appetitsaft*) begins to be secreted in thirty to forty seconds after beginning the meal, it increases and reaches its height in the last five minutes of the mastication, and diminishes after the first ten

<sup>13</sup> Paris médical, 1920, x, 286.



minutes of repose, and is absent a half hour after the termination of the sham meal. The acidity varies between 1.80 and 1.96, and the free acid between 1.64 and 1.80. The juice is rich in pepsin and in lab ferment. The method has been studied in pathological conditions.

(a) *Gastric Cancer*. The amount of juice withdrawn is about equal to that in health, but the acidity is always low and free HCl is often absent. Peptic digestion is below normal and coagulation of milk is slow.

(b) *Ulcer*. In ulcer of the walls or curvatures of the stomach, the juice is normal in amounts but is much increased in pyloric and pre-pyloric ulcers. There is always a hyperchlorhydria, even after cure, and the acidity is very high. Peptic activity is increased. Dupuy was able to distinguish one case of gastric syphilis from ulcer by the lower acidity.

(c) *Duodenal Ulcer*. There is hyperexcitability and exaggerated secretion.

(d) *Cholelithiasis with Dyspepsia*. There is hyperchlorhydria and increased peptic activity, and the fluid is often bile tinged.

(e) *Nervous Dyspepsia*. The author distinguishes three types of cases: (1) Neurasthenic-low activity, (2) delayed acidity, (3) mental anorexia—there is a notable diminution in the amount of juice secreted and a marked diminution in acid values.

(f) *Tubes*. Normal.

(g) *Alcoholism*. Of little interest now to the American medical public.

(h) *Tuberculosis*. Normal.

**Gastro-intestinal Diseases of the War.** Carles<sup>14</sup> is of the opinion that gastro-intestinal disorders were uncommon in soldiers at the beginning of the war, but with the hardships experienced in the field, and the nerve racking torments induced by "the prolongation of hostilities, the appearance on the battle field of barbarous instruments created by German savagery, gastro-intestinal disease, so rare at the beginning, became more numerous." Four categories comprise the gastropathies.

I. In the first may be placed all the true organic lesions—ulcer, stenoses, cancer, cirrhosis.

II. In the second, are classed the cases resulting from explosion and from gases. Hematemesis and melena due to rupture of blood-vessels by explosion and due to the irritant action (alteration of the mucous membrane) of gases.

III. In the third group are the cases of suprarenal insufficiency, caused by extreme muscular exertion. The common picture is that of atonic dyspepsia with constipation, associated with hypotension and pronounced asthenia, often showing the "white line" of Sergent. Medication is usually futile and the cases seem to recover in a remarkable way on daily or twice daily injections of one-half to one milligram of adrenalin.

IV. In the fourth category, the author places the gastro-intestinal neuroses "*pithiatiques de l'estomac*." The cure consists in isolation and

<sup>14</sup> Progres médical, October 18, 1919.

in reëducation—vomiting soon ceases, food may be eaten in comfort and those afflicted soon put on weight, all of which gain is lost when the soldier returns to trench life. In these individuals, radiographic examination reveals nothing, and the gastric chemistry is unaffected, but vomiting, loss of weight, emaciation, anemia, and the appearance of a grave illness continue. Emotionally these cases are hyperexcitable, the vasomotor state is out of equilibrium, there is much tremor and trembling with marked asthenia and exaggerated reflexes, so that the first impression is one of psychasthenia rather than of gastric nature.

V. To these four distinct groups, Carles adds a fifth in which there is naught but a painful sensation of fullness and of distention in the stomach after eating. These men have rushes of blood to the face, with vertigo, belching, flatulence, and a sensation of intracranial fullness of pulsations. An overwhelming desire to sleep after meals and an overweening tendency to fatigue are characteristic. Such a case seems at first blush to be a common gastric one, were it not for a group of symptoms which permit one to group such a one in the category of "sympathosis." These individuals have vasoconstriction of the extremities with cyanosis, a local sensation of coldness, congestion and peripheral sweating. There is also respiratory difficulty with attacks of tachycardia and instability of the pulse. Even a light meal will cause a discharge of all the gastric and nervous symptoms. The cause of the gastric disorders, etc., is to be found in a local irritation (true gastropathy) or in poisonous gas. The irritation of the sympathetic with its hyperexcitability is due to ascending inflammation, similar to the enteroneuritis cases described by Loeper and reviewed by me last year.

As far as the intestinal disturbances are concerned, they are far more involved than are the gastric cases, and fall into 7 groups:

1. Chronic enteritis following typhoid fever.
2. Rectosigmoiditis following paratyphoid fever.
3. Rectosigmoiditis due to dysentery or trench diarrhea.
4. Enteritis secondary to a bacillary peritonitis.
5. Parasitic enteritis (amebic).
6. Enteritis due to trichomonas, lamblia, etc.
7. Enteroneuritis.

Only the last-named needs comment! Last year the work of Loeper, a research of great value, was reviewed at length. It is believed by Loeper that each and every acute intestinal affection is followed by some intestinal disorder more or less serious, more or less banal, due to enteroneuritis, in much the same way as peripheral neuritis can eventually lead to change in the nerve roots, or as a carious tooth can cause trigeminal neuralgia. Even as in the latter case, pain persists though the cause be removed, so in the intestinal conditions, neuralgia or true neuritis continues after the disappearance of the intestinal disease. It is, in fact, a true sympathetic neuritis, due to fixation by this nerve of toxin or even intestinal organisms, and one may observe the nerve changes, degeneration, inflammatory, fibrous, in the nerve and ganglia of the plexuses of Auerbach, of Meissner and even the solar plexus.

There result long after the disappearance of the infectious or toxic

agency, digestive troubles expressed by diarrhea or constipation, spastic phenomena, pain, and by the common clinical syndrome known as mucomembranous enteritis.

**Gastric Ulcer.** Hurst<sup>15</sup>, in a paper putting forth new views on the pathology, diagnosis and treatment of gastric and duodenal ulcer, asks the question: "What is it about one individual that makes him liable to gastric ulcer, about a second that makes him liable to duodenal ulcer, and about others—the majority of people, that save them from being liable to either?" The greater curvature of the stomach with a standard opaque meal and with the patient in the erect posture, reaches the umbilicus, or a little below it; in some normal persons the stomach is *hypertonic*—the stomach curves obliquely to the pylorus, which is almost its lowest point, and the greater curvature is some distance above the navel, in some individuals the stomach is *hypotonic*—the stomach is hook-shaped, and the greater curvature is more than an inch below the umbilicus, the upper level of the gastric contents being correspondingly low. The hypertonic stomach generally empties itself more rapidly than the average normal one and the hypotonic stomach generally, but not so constantly, empties itself less rapidly.

The hypertonic stomach is associated with hypersecretion and the hypotonic stomach, although generally showing hyposecretion, may show hypersecretion. In duodenal ulcer the stomach is hypertonic and empties itself with unusual rapidity, the onset of pain corresponding with the moment when the stomach is almost empty. In gastric ulcer the stomach is somewhat hypotonic and almost invariably empties itself more slowly than the average normal. Hurst believes the hypertonic stomach seen in duodenal ulcer persists many years after cure and after many years of complete freedom from symptoms, and he thinks that the characteristic x-ray appearance is not due to the ulcer, but that it represents a type of stomach, and he propounds the theory that there is one type of stomach in which a duodenal ulcer will develop, if the necessary exciting causes are present, a type in which gastric ulcer will develop, and a type in which there will be no ulceration despite the exciting causes. He has seen no instance of gastric and duodenal ulcer in members of the same family, it is either gastric in each member or duodenal, is not gastric in one member and duodenal in another, and this leads him to believe that the types of stomach which predispose to the development of gastric and of duodenal ulcer respectively are congenital gastric ulcer or duodenal ulcer diathesis.

Hurst reviews at some length the exciting causes of ulceration—infection, trauma—but the occurrence of ulceration is rare, he says, in comparison with the frequency of the exciting causes, because it is unlikely for the injured mucous membrane to be digested by the gastric juice unless there is the predisposing type of stomach. In the gastric ulcer type not only is the acidity high but the emptying of the stomach is slow, so that an extremely strong juice remains in contact with the mucous membrane for an exceptionally long time, and the passage of

<sup>15</sup> British Medical Journal, April 24, 1920, p. 559.



acid chyme through the duodenum is so slow and intermittent that the alkaline duodenal contents are capable of neutralizing it to a great extent. In the duodenal ulcer type the first part of the duodenum is kept constantly filled with exceptionally acid chyme and neutralization is impossible; even when the stomach is empty, gastric juice is secreted and passes rapidly into the duodenum without being diluted and without being partially neutralized by admixture with food. Hurst believes the tendency to duodenal ulcer is aggravated by smoking, the nicotine increasing the hypertonus and hypersecretion by acting on the autonomic nervous system. In discussing diagnosis, Hurst quotes extensively from Moynihan so that the latter's opinions will be inserted here and the abstract of Hurst's article will be resumed later on.

We owe most of our knowledge of gastric and duodenal ulcer symptomatology to Moynihan and to the Mayo brothers. Moynihan,<sup>16</sup> in the paper under review, deals entirely with chronic gastric ulcer.

"A gastric ulcer is, of course, an ulcer occurring in the stomach. During development the stomach is differentiated as one part of the foregut from that other part which forms the duodenum as far down as the ampulla of Vater. The foregut terminates at the point of entrance of the ducts of the liver and pancreas; at the end of the second month of fetal life the pylorus marks off the stomach from the duodenum. When development is complete, it is, as a rule, easily possible in all periods of life to distinguish the stomach from the duodenum. On palpation the pyloric muscle and valve are felt at once. Exactly in the line of the pylorus a thin white line is to be seen on careful examination; the line becomes clearer if in the living subject the pylorus is held forward by a finger and thumb placed, one on the stomach the other on the duodenum, and closed to meet in the pylorus. In close proximity to the 'pyloric vein,' which begins at or near the middle of the anterior surface of the pylorus and runs downward to the greater curvature. The 'pyloric vein' is constant, its arrangement variable. It may be single and large, short and branched, or long with only very slender branches; it may be double; it may or may not be met by a smaller vein running up toward the lesser curvature; it may lie on either side of the pyloric white line. The perfectly fair criticism has been made against the acceptance of this vein as a landmark, that veins are very irregular in their arrangement, position, and distribution, and that nowhere else in the body is the position of a vein so constant as this is asserted to be. And it must be frankly admitted that there is a very small number of cases in which the venous arrangement is such that no accurate localization of the pylorus is possible from a surface inspection. But there is no landmark in the body that is invariable. For many years past I have drawn the position of this vein as seen during an operation while the parts were under inspection, and it is quite safe to say that in at least 90 per cent. of the cases the markings I have mentioned may be accepted as accurate. Latarjet,<sup>17</sup> after a research conducted for the purpose of deciding the value of the vein as an accurate landmark, concludes in favor of its acceptance.

<sup>16</sup> British Medical Journal, December 13, 1919, p. 765.

<sup>17</sup> Lyon Chirurgical, 1911, p. 337.

"An ulcer occurring on the proximal side of this vein is a 'gastric ulcer;' an ulcer occurring one-quarter inch or one-half inch or more beyond it is a 'duodenal ulcer.' It is not merely a matter of academic interest to distinguish them; their symptoms are sufficiently distinct to allow an accurate diagnosis of duodenal ulcer to be made with remarkable constancy; their complications and sequels in respect of perforation and hemorrhage are very different; cancer develops often upon the base of a gastric ulcer, and almost never upon the base of an ulcer in the duodenum. Gastric ulcer is a disease of comparative rarity; its diagnosis from the clinical evidence alone is difficult; its mimicry by other conditions extremely frequent.

"These statements may not find a ready acceptance everywhere. For if the text-books of medicine, or the special works of distinguished authors are read, or if the diagnoses made in the out-patient medical clinics are reviewed, it will be found that there is a general agreement that gastric ulceration occurs frequently, and that its symptoms are of a kind hardly admitting of doubt or difficulty in diagnosis. I have spent a great deal of time in reading almost everything to which I could obtain access that has been written about gastric ulcer, and I am compelled to say that when the statements universally made are tested by the experience gained in the operation theater they are found to be inaccurate. My contention is that a full, clear, and truthful description of the symptoms of gastric ulcer is rarely given; and that the conditions described as 'gastric ulcer' are, in the majority of cases, indicative of other disease."

Ulcer of the stomach occurs twice as often in men as in women, and its chief symptom is *pain* and the latter's chief attribute is regularity. There are periods of intermission to be sure, but when the attacks are present the pain always displays regularity. It comes after all meals and the interval between eating and the onset of pain is fairly constant. The earlier the pain is felt after a meal the nearer is the ulcer to the esophagus, if pain comes one or one and a half hours after eating, the ulcer is prepyloric, if it comes two, three or four hours after a meal, the ulcer lies beyond the pylorus, and until stenosis, subacute perforation or adhesions develop, the period of relief after a meal is invariable, but the above complications lead to a delay of pain in gastric ulcer and to a premature discharge of distress in duodenal ulcer. The pain in gastric ulcer disappears after an hour while in duodenal ulcer it increases until the meal is taken—a heavy meal causes pain of gastric ulcer to appear earlier and delays the pain of duodenal ulcer. The pain is variously described as deep, boring, burning, aching, gnawing or it may be described as a desire for food and warmth. It is situated on the left side, is high in the epigastrium and in some severe cases there is much pain in the back, especially when the ulcer is on the lesser curvature, or on the posterior wall.

The position of the ulcer, its freedom from adhesions to neighboring parts both affect the type of pain, with its periods of latency and its time of onset after meals. When small and high on the lesser curvature or just on the posterior surface, symptoms are of shorter duration and recur. If



the ulcer is large, excavating the liver or burrowing into the pancreas, or if fixed by adhesions to the abdominal wall or liver, the symptoms are less likely to be intermittent. If, in addition to the above, there are wasting and anemia, one should suspect malignancy. Patients with gastric ulcer find that three heavy meals a day bring their own punishment and therefore they learn to eat lighter meals at shorter intervals and thus do not show loss of weight. Often prostration, feebleness or lassitude precede by weeks and months the onset of actual pain, and the periodicity of the two is the same.

The next symptom emphasized by Moynihan is *vomiting*, which unless there is obstruction is an inconspicuous feature. "When in the record of any patient suffering from 'dyspepsia' there is a story of frequent vomiting, of the inability of the stomach to tolerate the presence of any foods, of even fluid nourishment sparsely taken being at once rejected, the thought that gastric ulcer is the cause should be driven from one's mind. That type of history which is commonly heard is, I find, rarely present in organic disease of the stomach."

*Hematemesis* occurs far less commonly than is supposed, and blood manifested as melaena or in the vomit is recorded in less than 25 per cent. of his cases. Moynihan acknowledges of course, that bleeding in ulcer does occur, but when hemorrhage is seen, he thinks first of splenic anemia, cirrhosis of the liver, appendicitis and other infective conditions, rather than of gastric ulcer. Summing up the symptomatology, Moynihan places the chief dependence on one symptom—pain. He admits the great advantages to be derived from *x-ray* examinations and his technician follows the method of Carman of the Mayo clinic. He is unenthusiastic about gastric analysis and also about physical examination. He regards the diagnosis as eminently difficult and attention is directed to his article "Disappointments after Gastro-enterostomy," abstracted elsewhere in this monograph, in order to show how frequently patients are subjected to operations because of mistaken diagnosis.

Speaking of medical treatment, he approves of the method of Sippy, and he says that gastric ulcers undoubtedly heal but they do not remain healed, and if they heal they heal with some deformity—hour-glass contraction and pyloric obstruction. Notwithstanding this opinion, he believes that serious medical treatment should be tried in all cases of chronic gastric ulcer, and to keep him on medical treatment until the *x-ray* has shown that it is healed.

To return to Hurst's paper. Patients with symptoms of ulcer but without the typical *x-ray* findings, he believes are suffering from a pre-ulcerative condition, which will certainly lead to actual ulceration in time, unless the exciting causes as infection, trauma, etc., are removed. The teeth should be put in perfect order, and should be examined every six months, the pharynx and sinuses should receive attention; the appendix should be removed if there is evidence of chronic inflammation, and at the time of operation, the stomach, duodenum and gall-bladder should be inspected, but under no circumstances should a gastro-enterostomy be performed unless there is actual ulceration (see Moynihan, "Gastro-enterostomy"). The patient should be made to understand



the dangers he must run of having an ulcer develop unless he eats slowly, chews his food thoroughly and avoids irritating food and drink. Smoking should be permitted, if at all, only in strict moderation.

With the gastric ulcer type of stomach, which empties itself slowly, three good meals without any intermediate feeds, should be taken, but with the duodenal ulcer type of stomach, which empties itself too rapidly, a tablespoonful of olive oil should be taken before each of the three chief meals, and intermediate eating is allowed.

All the above Hurst urges as prophylactic measures. Under medical treatment he reviews extensively the Sippy treatment which is so well known to readers of *PROGRESSIVE MEDICINE*.

**THREAD TEST OF GASTRIC ULCER.** Koelensmid<sup>18</sup> remarks that Einhorn's thread is a very sensitive test for occult blood in the stomach. But a positive diagnosis does not necessarily indicate an ulcer. In 160 applications of the test, the findings very rarely conflicted with what was known of the stomach conditions otherwise. In 3 cases of cancer there was no reaction; in 61 cases of certain ulcer in stomach or duodenum, the reaction was positive in 44; negative in 2, and dubious in 15. In 43 cases of neurosis, atony, or other non-ulcer cases, the reaction was negative in 31, dubious in 10, and positive in 2. The test thus has strong corroborative value, and repeated negative reactions render the diagnosis of ulcer in stomach or abdomen highly improbable.

**EROSIONS OF THE STOMACH AND VAGAL IRRITATION.**<sup>19</sup> The vegetative or autonomous peripheral nervous system, consisting of the vagus and the sympathetic, comprises within itself antagonistic entities, holding each other normally in equilibrium. The antagonistic relation between the sympathetic and vagus results in that paralysis of the sympathetic, produces the same symptoms as irritation of the vagus and *vice versa*. There are a number of substances which act as irritants or paralyzers of these nerves—thus atropin paralyzes the vagus while epinephrin irritates the sympathetic, definite sympathetic paralysis being unknown. The vagus being the secretory and motor nerve of the stomach, hypersecretion, hyperchlorhydria, pyloric spasm are thought to result from irritation of the vagus (vagotony). These symptoms resembling those of gastric ulcer have led certain writers to believe that ulcer is but an expression of a vagotonia. Petrin and Thorling studying patients with ulcer, and their reaction to pilocarpin and atropin on the one hand, and epinephrin on the other, concluded that vagotony is frequently present in patients with ulcer and a sympatheticotony but rarely. Finzi whose work was quoted in *PROGRESSIVE MEDICINE*, December, 1914, p. 26, believed there were changes in the circulation after adrenalectomy, which changes led to necrosis and ulceration. Nicolaysen believes in Finzi's clinical study of 5 cases but an analysis of these 5 seemed to me in 1914 to be inconclusive. Friedmann<sup>20</sup> believes in the undoubted endocrine origin of peptic ulcer, and leans to the belief that both the thyroids and adrenals are at fault. According to Nicolaysen, the work

<sup>18</sup> Abstract, Journal of the American Medical Association, 1919, lxxiii, 948.

<sup>19</sup> Nicolaysen: Arch. Int. Med., 1920, xxv, 295.

<sup>20</sup> *PROGRESSIVE MEDICINE*, December, 1919, p. 27.

of the authors quoted above, shows that stimulation of the vagus or paralysis of the sympathetic may cause changes in the lining of the stomach.

He has produced in rabbits, by means of pilocarpine injections, a definite erosion of the gastric mucosa, which is preceded by an extravasation of blood due to the irritation of the vagus. He believes the hemorrhage is not of a vasomotor nature because of the sympathetic innervation of the vessels of the stomach, but he inclines to the supposition that contraction of the musculature of the stomach, especially the muscular mucosa, through which the small vessels to the mucous membrane pass, cause the bleeding. The hemorrhage causing damage of the mucosa, erosion follows by digestion of the tissue, and the extent and depth of loss of tissue depends upon the extent of the hemorrhage. There was no increase in acidity as is generally believed after pilocarpine, but rather diminished acidity, perhaps due to the large quantities of mucus which are poured out.

**SIPPY TREATMENT OF ULCER.** Friedenwald and Morrison<sup>21</sup> have employed this method of treatment in 452 cases controlling the diagnosis and end-result by the usual *x*-ray examination and the customary clinical tests. Forty-nine cases were unable or unwilling to follow the treatment for more than a few days, so 403 cases are analyzed in this paper. These are divided into three groups.

Group I. 183. The milder cases which probably would have recovered under any form of treatment.

Group II. 118. The moderately severe cases which presented symptoms extending over a long period of time, in which such symptoms as pain, hemorrhage, or vomiting were prominent.

Group III. 102. The severe cases, comprising those patients who had followed other forms of treatment unsuccessfully, whether medical or surgical, or those associated with persistent and recurrent hematemesis or melena, or had had severe pylorospasm or evidences of partial obstruction.

Group I. Of the 183 cases, 172, or 94 per cent., were cured, while 11, or 6 per cent., were not cured. Five of the cases presented no evidences of healing and 6 had to be operated upon.

Group II. Of the 118 cases, 101, or 85 per cent., were cured, while 17, or 15 per cent., were not cured.

Group III. Of the 102 cases in this group, 38 had already been treated by medical methods; 15 had had operations; 24 had recurrences and 25 had signs of partial obstruction. Of the total number, 82, or 80 per cent., were cured, 15, or 14 per cent., were not cured, and 5, or 5 per cent., died.

When one compares these results with those of other forms of treatment, there appears to be a marked advantage in favor of the Sippy cure. Friedenwald and Morrison have already reported 72 per cent. cures with the Leube method, 66 per cent. by the Lenhartz, and 50 per cent. when treated as ambulatory cases. At the end of three years or longer, 94 were followed up and 68, or 72 per cent., were well, while 26,

<sup>21</sup> Southern Medical Journal, 1920, xiii, 318.



or 48 per cent., had had relapses. The authors believe relapses are generally due to indiscretions in diet, following the cure and on this account the diet of the patient should be carefully regulated, acids and indigestible foods should be prohibited and alkalies administered for a considerable length of time after the "cure" has been completed. The following diet list presents their method of feeding during the Sippy cure. Either sodium bicarbonate, gr. x, with magnesium calcined, gr. x, or sodium bicarbonate, gr. xx, with bismuth subcarbonate, gr. x, are given alternately on the half hour, from 7.30 A.M. to 10.30 P.M. If there is excessive secretion present at night, this is removed by aspiration. The patient remains in bed for three to four weeks. In the first diet list, milk and cream means 3 ounces of a mixture of equal parts milk and cream. The total bulk of each feeding should be not over 6 ounces. Modified Sippy diet followed in some cases of peptic ulcer:

Milk and cream, equal parts, 1½ oz. every hour from 7 A.M. to 7 P.M. nine to twelve days.

HOUR	DAYS				
A.M.	1st to 5th	6th	7th to 8th	9th to 10th	11th to 14th
7.00	Milk and cream	Soft egg, Milk and cream	Milk and cream	Cereal, Milk and cream	Soft egg, cereal, Milk and cream
8.00	Milk and cream	Milk and cream	Milk and cream, soft egg	Milk and cream	Milk and cream
9.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
10.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
11.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
12.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
P.M.					
1.00	Milk and cream	Milk and cream	Cereal, egg, milk and cream	Cereal, egg and cocoa	Egg, cocoa and custard
2.00	Milk and cream	Milk and cream	Soft egg, milk and cream	Milk and cream	Milk and cream
3.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
4.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
5.00	Milk and cream	Milk or cocoa, soft egg	Cereal, milk and cream	Milk toast, egg and cocoa	Milk toast, egg and cocoa
6.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
7.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	Milk and cream
Milk and cream each 1½ oz.					
A.M.	15th	16th	17th to 18th	19th	
7.00	Egg, cereal, milk and cream	Egg, cereal, milk and cream	Soft egg, cereal, cocoa	Milk and cream	
8.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	
9.00	Milk and cream	Milk and cream	Milk and cream	Chicken broth	
10.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	
11.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	
12.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	
P.M.					
1.00	2 eggs, cocoa, milk toast	Cream-milk, toast, egg, vanilla ice- cream	Minced chicken, milk, milk toast, vanilla ice-cream	Minced chicken, cocoa, dry toast, vanilla ice-cream	
2.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	
3.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	
4.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	
5.00	Milk toast, egg, cocoa	Milk toast, egg, cocoa	Milk toast, egg, cocoa	Milk toast, egg, cocoa	
6.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	
7.00	Milk and cream	Milk and cream	Milk and cream	Milk and cream	
Milk and cream each 1½ oz.					
A.M.	20th	21st	22d on		
7.00	2 eggs, cocoa, 1 slice dry toast, butter	2 eggs, 1 slice of butter	of toast, Milk and cream		
8.00	Milk and cream	Milk and cream	Milk and cream		
9.00	Milk and cream, egg	Milk and cream, egg	Cereal, milk and cream, egg		
10.00	Milk and cream	Milk and cream	Mild and cream		
11.00	Broth	Milk and cream	Milk and cream		
12.00	Milk and cream	Milk and cream	Milk and cream		



HOURL	20th	DAYS	21st	22d on
1.00	Minced chicken, 1 slice dry toast, butter, cocoa, spinach	1	broiled lamb or mutton chop, dry toast, cocoa, butter, asparagus or baked potato	Chop or minced chicken, dry toast, strained vegetable or baked potato, cocoa butter
2.00	Milk and cream		Milk and cream	Milk and cream
3.00	Broth		Milk and cream or milk and egg	Milk and cream
4.00	Milk and cream		Milk and cream	Milk and cream
5.00	2 eggs, cereal, milk toast, cocoa		2 eggs, cereal, milk toast, cocoa	Stewed fruit or baked apple, 2 eggs, cereal, milk toast, cocoa
6.00	Milk and cream		Milk and cream	Milk and cream
7.00	Milk and cream		Milk and cream	Milk and cream
Milk and cream each 1½ oz.				

A.M.	P.M.	MEDICINES	
7.30	1.30 . . . . .	} Heavy calcined magnesia . . . . .	gr. x
9.30	3.30- 5.30 . . . . .		Sodium bicarbonate . . . . .
11.30	7.30- 9.30 . . . . .	} Bismuth carbonate . . . . .	gr. x
8.30	12.30- 2.30 . . . . .		Sodium bicarbonate . . . . .
10.30	4.30- 6.30 . . . . .	} Bismuth carbonate . . . . .	gr. x
	8.30-10.30 . . . . .		Sodium bicarbonate . . . . .
Three to four days following:			
7.00	3.00 . . . . .	} Milk and cream . . . . .	āā oz. iss
11.00	7.00 . . . . .		
9.00	1.00 and 5.00 . . . . .	Milk and egg or cocoa	

MEDICINES										
7.30	3.30	.	.	.	.	.	.	}	Heavy calcined magnesia . . . . .	gr. x
11.30	7.30	.	.	.	.	.	.		Soda bicarbonate . . . . .	gr. x
9.30	1.30	.	.	.	.	.	.	}	Bismuth subcarbonate . . . . .	gr. x
	5.30	.	.	.	.	.	.		Soda bicarbonate . . . . .	gr. x
	9.30	.	.	.	.	.	.			
Four to five days following:										
7.00-11.00	3.00- 7.00.	.	.	.	.	.	.	}	Milk and cream . . . . .	āā oz. iss
9.00	.	.	.	.	.	.	.		Oat meal, egg and cocoa	
	1.00 and 5.00	.	.	.	.	.	.		Milk toast, egg and cocoa	

		MEDICINES			
7.00	3.00	. . . . .	}	Heavy calcined magnesia . . . . .	gr. x
11.30	7.30	. . . . .		Sodium bicarbonate . . . . .	gr. x
9.30	1.30	. . . . .	}	Bismuth subcarbonate . . . . .	gr. x
9.30	5.30	. . . . .		Sodium bicarbonate . . . . .	gr. x
To be followed for some weeks.					
7.00	3.00- 7.00	. . . . .	}	Milk and cream . . . . .	āā oz. iss
11.00		. . . . .		Milk and egg or cocoa . . . . .	
9.00	1.00- 5.00	. . . . .	Soft diet without acids		
7.30	3.30	. . . . .	}	Heavy calcined magnesia . . . . .	gr. x
11.30	7.30	. . . . .		Sodium bicarbonate . . . . .	gr. x
9.30	1.30	. . . . .	}	Bismuth subcarbonate . . . . .	gr. x
	5.30	. . . . .		Sodium bicarbonate . . . . .	gr. x
	9.30	. . . . .	As required, additional sodium bicarbonate . . . . . gr. x to xx		

In man, hemorrhagic erosions occur in the stomach and duodenum. They are superficial and usually have a hemorrhagic floor. These human erosions resemble those produced experimentally (Nicolaysen has numerous photographs to illustrate his work), but the question remains whether hemorrhagic erosions in man depend on vagus irritation. He quotes 10 cases and without examination of the vagus nerves and the nerves of the stomach, he concludes that there had been vagal irritation. Six of these cases had brain or meningeal disease, three had chest conditions and one had peritonitis, and because of the location of the disease, and the occasional occurrence of a slow pulse, he accepts the possibility of there having been vagal irritation. The concluding part of Nicolayson's paper is weak and his studies of human material do not warrant a leap toward such conclusions. His animal experiments are interpreted correctly, no doubt, but the clinical cases have been insufficiently studied and scarcely add to the lesson he has drawn from his work with rabbits.

INTERNAL TREATMENT OF GASTRIC ULCER. Ohnell<sup>22</sup> reports experiences which differ from the usual in that gastric ulcers showing a finger-like pocket or niche with the contrast meal healed definitely under internal treatment alone. The niche is usually accepted as an indication for operation. In 36 certain and 2 probable cases, the narrow pocket disappeared as the ulcer healed. In 3 other cases, the pocket grew very much smaller. There has been no recurrence in any instance during the six to eighteen months since. The reason why internal treatment does not give such good results in the hands of others, he explains is probably because the treatment is not kept up long enough. The different features of the 56 cases are tabulated under twenty-six headings, and the roentgen findings in each are reproduced. The tests for occult blood were negative, as a rule, in the cases in which the niche disappeared under internal treatment. The smallest niche shadow was 4 by 3 mm.; the widest 55 by 16, and the deepest 6 by 28 mm. The niche region was tender before or during the treatment but not in any case after completion of the course of treatment. Radioscopy of the stomach with the patient in different attitudes shows the widely different positions assumed by the stomach, with consequent traction, and on this account he keeps the patient absolutely still on his back for four weeks, and keeps him in bed for a further two weeks.

If the patient wearies of lying on his back and finds it difficult to sleep in this position, he gives a little sedative by the rectum the first few nights. This aids further in reducing peristalsis during the first three or five days in which nothing is allowed by the mouth, and the extremely cautious resumption of food thereafter. Moist heat is applied with fomentations for about a month; then he changes to cotton, and when the patient gets up this is changed for an abdominal band. Fluids are supplied copiously by the rectum, 10 per cent. grape sugar solution, 6 per cent. honey, or 0.9 per cent. sodium chlorid. He began with 400 gm. three times a day, reducing the amount proportionally as feeding by the mouth is resumed, never letting the fluid intake drop below one liter a day. To ward off thrombosis, the patients are made to change

<sup>22</sup> Abstract, Journal of the American Medical Association, 1919, lxxiii, 1736.

the position of their legs repeatedly. Hygiene of the mouth is enforced. He had no parotitis develop in any instance. The bowel movements are promoted by an enema on alternate days. The patient is warned not to strain. It is better to let feces accumulate than to strain and hinder healing at first. The diet is 30 gm. milk seven times a day, repeated the seventh day plus the yolk of an egg. But 400 gm. 10 per cent. sugar solution are given by the rectum three times a day from the first day on. Then two rectal injections are made, and the seven milk feedings total 630 gm. with two yolks. The fourteenth day the rectal injections are dropped, and 180 gm. of milk are fed seven times, plus four yolks. The fourteenth day, 210 gm. of milk seven times a day and five yolks, and after this two to five soft boiled eggs, zwieback and butter

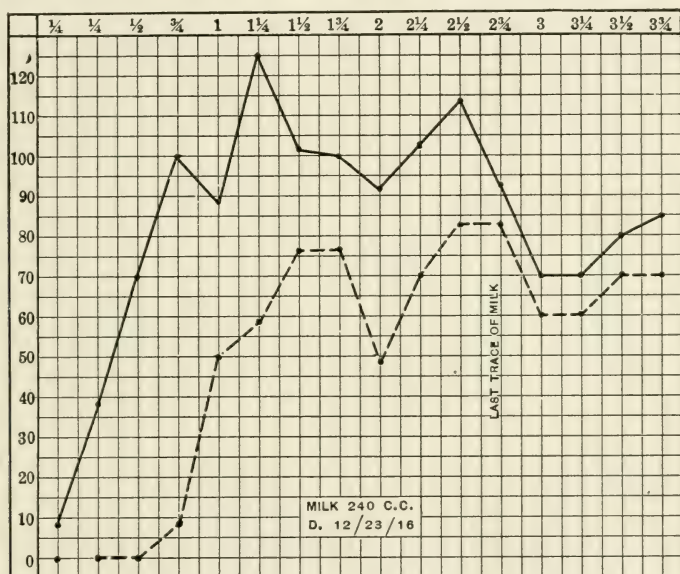


CHART I

are given with up to 1500 gm. milk in five feedings. The course takes a full month. His experience confirms that a roentgen niche may be due to a deformed but not ulcerated part of the gastric mucosa.

**EFFECTS OF RESTRICTED (SO-CALLED ULCER) DIETS UPON GASTRIC SECRETION AND MOTILITY.** The problem which Crohn and Reiss<sup>23</sup> set for themselves was the study of the chemism and motility of the stomach in ulcer patients, who were receiving ulcer diets (unmodified Lenhartz diet, or a diet similar to Sippy's). Upon admission, the patients were subjected to careful examination, physical and chemical, including the fractional gastric analysis. After the collection of all data, the patient was placed upon a restricted diet for from two to four weeks. Fractional analyses were made every few days. Thirty-four patients were included in their series, 5 of whom had ulcers, demonstrated later by operation,

<sup>23</sup> American Journal of the Medical Sciences, 1920, clix, 70,



21 were diagnosed clinically as ulcer, and 8 were thought to have a gastric neurosis or a functional disturbance of the stomach.

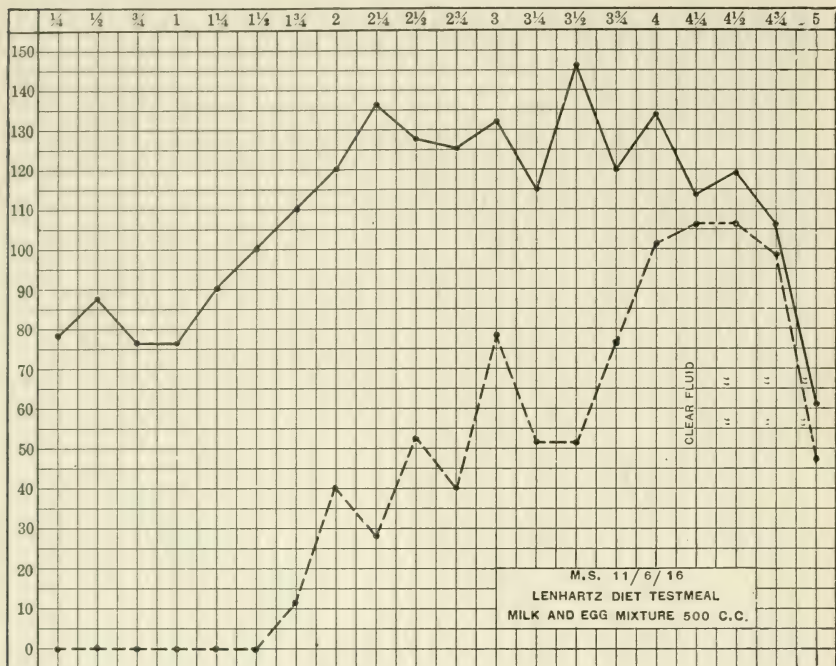


CHART II

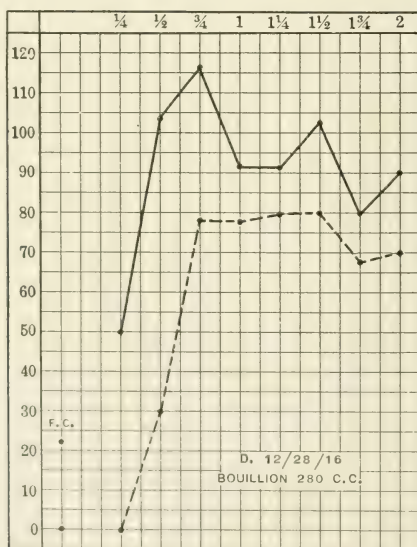


CHART III

The Lenhartz dietary was used unchanged, the Sippy was employed with the following modification: milk and cream in small doses (2 to 3 ounces), were given hourly during the day for the first three days; cereals were then added twice daily. At the end of a week two eggs a day were

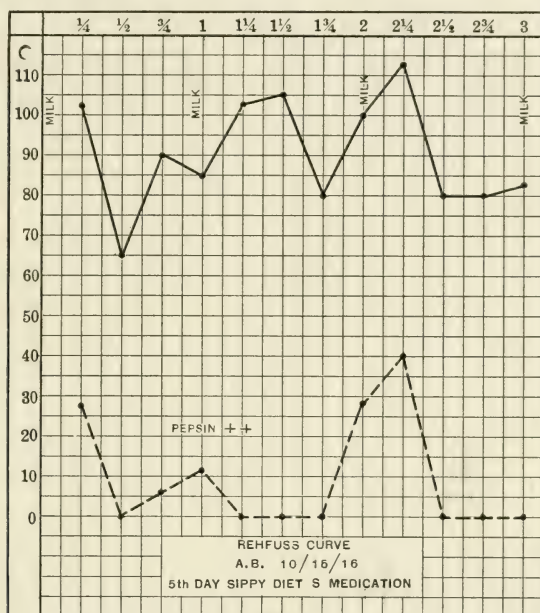


CHART IV

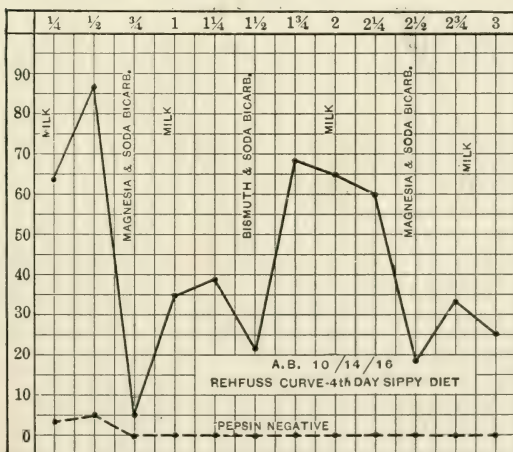


CHART V

added, and pureed vegetables were gradually introduced. All forms of meat were withheld until the third week. Antacids in small quantities were given between feedings, bismuth being a constant component of these powders. Occasionally lavage for gastric stasis was employed.

Chart I shows the curve after giving 240 c.c. of milk. It will be seen that milk causes a high total acidity up to 128 c.c.  $\frac{N}{10}$  NaOH. The height of the acidity is maintained for three or four hours, free acid

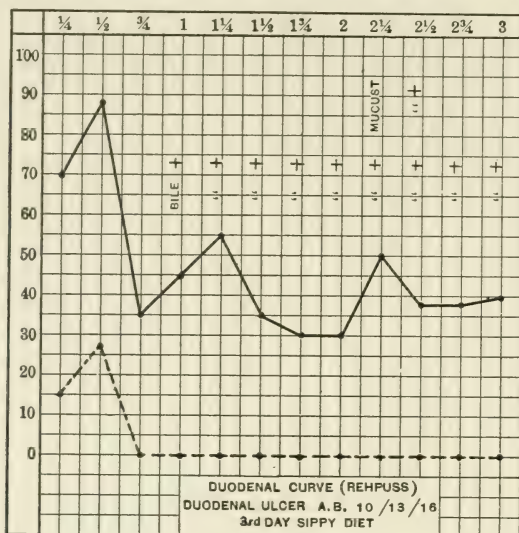


CHART VI

is present in larger quantities than is encountered with cereal or bread test-meals and the stomach takes considerably longer to empty itself. The acid binding property of milk is apparent in only the first half hour, after which time free acid is present in liberal amounts.

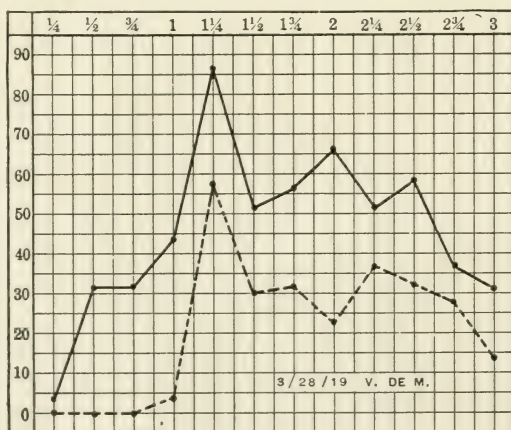


CHART VII

Chart II shows the effects of a combination of milk and eggs. The total acid curve is still higher (146 per cent.), free acid becomes evident just after one and one-half hours but is present in large amounts during



the remainder of the digesting cycle. Emptying time is prolonged and a free hypersecretion persists after the disappearance of food.

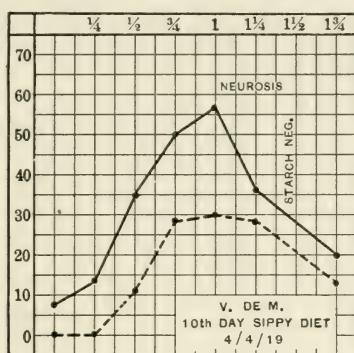


CHART VIII

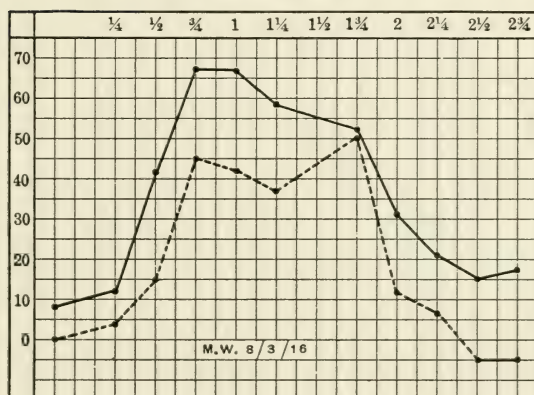


CHART IX

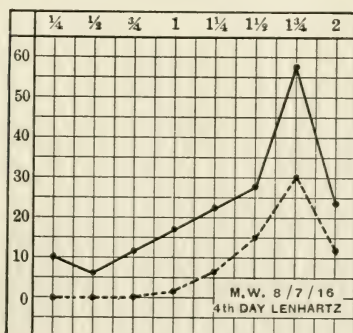


CHART X

Chart III shows the reaction to 280 c.c. of clear bouillon. No considerable binding of acid is at any time demonstrable. A higher acidity both free and total, quickly takes place and is maintained for two hours after which time the stomach is empty. The authors conclude from

these preliminary studies that milk is a strong acid stimulant and is emptied only slowly through the pylorus; the combination milk and egg is a powerful gastric stimulant, causing hyperacidity and hypersecretion, with prolongation of the emptying time; bouillon fails to bind acid and is a mild digestive stimulant.

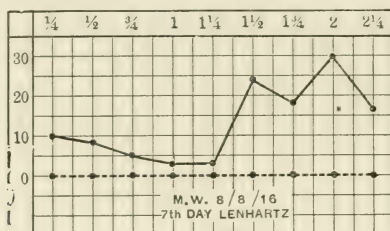


CHART XI

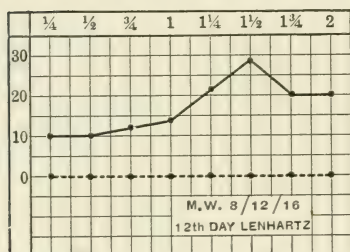


CHART XII

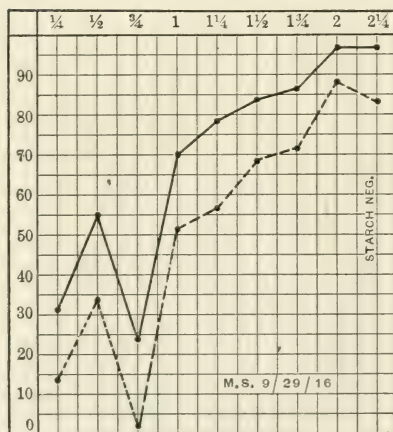


CHART XIII

Chart IV illustrates the effect of frequent repetition of food. Milk was given hourly, and whereas the total acid remains moderately high, very little free acid is allowed to accumulate. As the free acid rises toward the conclusion of each 15-minute period, it meets the new portion of milk and is immediately combined. Since peptolytic digestion

occurs only in the presence of free acid, it is apparent that the stomach is really inactive as far as the actual splitting of the protein molecule is concerned. If to the hourly portion of milk is added an alternating small dose of bismuth-soda and magnesia-soda in 5-grain doses free acid disappears and the total acidity is lowered. (See Chart V.)

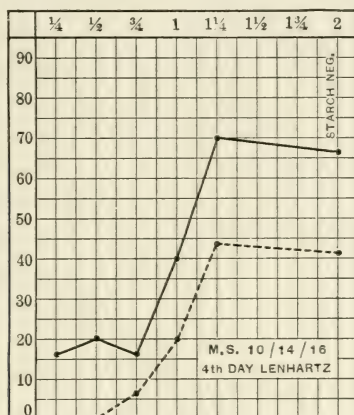


CHART XIV

Therefore if the reduction of total acidity and complete neutralization of free HCl were the aim of an ulcer treatment then the plan of alternate milk and antacids meet all the requirements. But there is considerable doubt in the minds of many that gastric ulcer is due to the local corrosive action of the gastric juice. Chart VI shows a duodenal curve and here we note no high total acidity and no free acid. Nevertheless duodenal ulcers do occur despite this very desirable condition of anacidity.

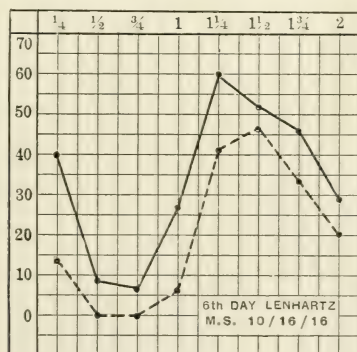


CHART XV

EFFECT OF MEDICAL TREATMENT ON GASTRIC ACIDITY. Of Crohn and Reiss's 34 patients, 11 had an isosecretory and 23 a hypersecretory curve. Medical treatment succeeded in lowering the acid curve in 6 of the 11 cases with rise of iso- or hyposecretory curves and 5 were unaffected. Of the 23 other cases, 7 showed a lowering of the acid curve, 16 remained unchanged.



Chart XIII is the curve of a case of functional hyperacidity before treatment, and Chart XVI the same case on the tenth day of a Lenhartz diet. There is marked lowering of activity, diminution of hypersecretion and improvement in motility.

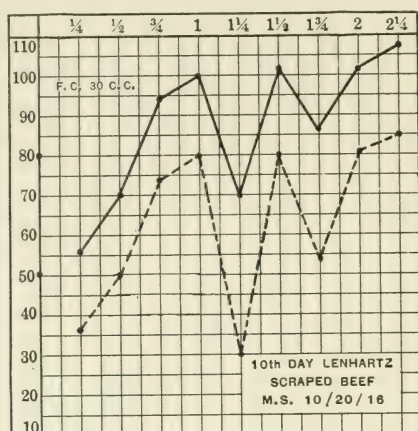


CHART XVI

Chart IX is the curve before treatment of a probable duodenal ulcer and Chart X is the curve of the same patient on fourth day of Lenhartz. Chart XI on the second, and Chart XII on the twelfth day. The progressive lowering of acidity was accompanied by gradual improvement of subjective symptoms and disappearance of pressure tenderness. In this patient there was chemical improvement as early as the fourth day of treatment, which differs from the majority of cases who show no improvement until the fifth or seventh day.

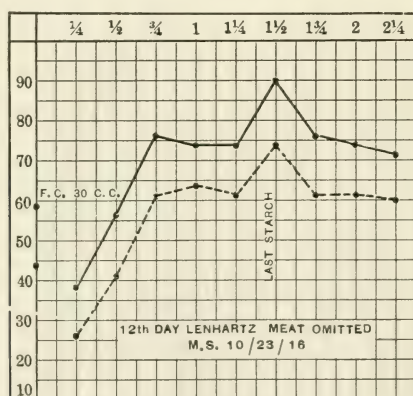


CHART XVII

Twenty-one cases showed no improvement in their curves. Charts XIII, XIV, XV, XVI, XVII and XVIII are from the same patient showing the change of curve after the giving of meat, with the persistent hyperacidity which followed. Charts XIX and XX are still from the same patient, at a later period in the treatment.

The question which naturally arises is whether reduction of the hyperacid curve is accompanied by clinical improvement, and conversely, is a resistant hyperacid curve associated with persistent gastric distress? In the author's series, 13 were chemically improved, 21 not, and improve-

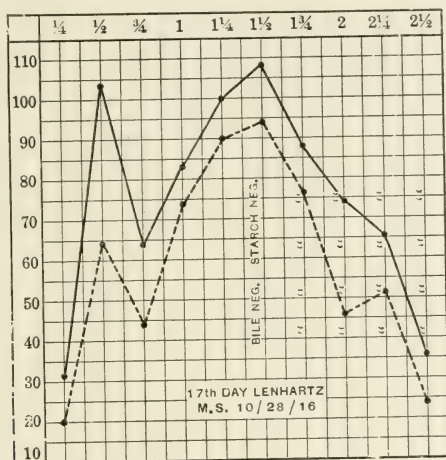


CHART XVIII

ment in only 38.3 per cent. of the cases. Clinically, however, 25 of the 34 cases were discharged free of symptoms (73.5 per cent.). Of the 13 chemically improved cases 12 left the hospital symptomless. Of the 21 cases with a persistently high curve despite treatment, 13 (62 per cent.) were markedly improved clinically, the remaining 8 cases (38 per cent.) were clinically unimproved.

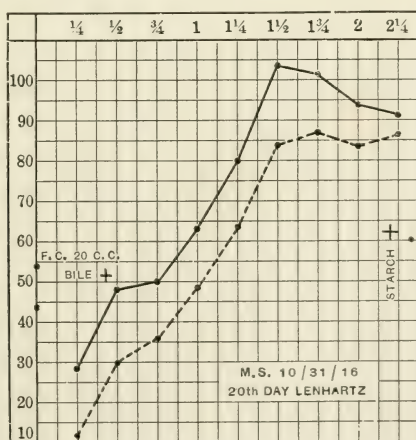


CHART XIX

EFFECTS OF DIET AND REST IN BED UPON HYPERSECRETION. Hypersecretion is a common phenomenon in ulcer, and was present in this series twenty times. In 16 of these cases, hyperacidity accompanied

the hypersecretion. In 9 of the 20 cases (45 per cent.) hypersecretion was improved or made to disappear, in the other 11 (55 per cent.) no improvement was noted. There was little relationship between clinical improvement and chemical finding for while in 11 cases (55 per cent.) the hypersecretion was unaffected, yet 16 of the 20 (80 per cent.) were clinically improved and free of symptoms.

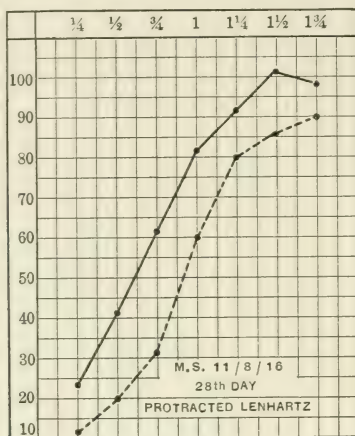


CHART XX

*Effect on Motility.* Using 500 c.c. of thick oatmeal gruel as a test breakfast, normal motility with the fractional method may be regarded as one and three-quarters to two hours. In the series of 34 cases of ulcer or suspected ulcer, there were 13 instances of delayed motility. In all but two of the series the emptying time was definitely shortened (85.4 per cent.) and still more striking is, that clinical improvement and improvement in motility went hand in hand. A reduction in acidity did not always accompany motility improvement. Thus of the 11 cases with improved emptying time, in only 3 was hyperacidity improved, while in the remaining 8 the high acid curve persisted. (There are several errors in calculation in the article under review, which I have tried to correct. Should my substitution for the figures given by Crohn and Reiss be inaccurate, the reader may censure the reviewer rather than blame the authors.) Hypersecretion was noted 6 times in connection with delayed emptying and in 4 of these it was not relieved by the treatment.

*Discussion.* Clinical improvement can take place, in the opinion of Crohn and Reiss, irrespective of improvement in acidity, secretion or motility. The relief from subjective pain is doubtless associated with lessened violence of hunger contractions. The fact that in a large proportion of cases, hyperacidity and hypersecretion could not be controlled, while in a small proportion this aim was achieved leads the authors to believe that in certain cases, ulcer treatment is not continued long



enough, that there is too soon a return to solid food like meat, which, in the Lenhartz diet is given on the tenth day.

**GASTRO-ENTEROSTOMY.** *Disappointments After.* Moynihan,<sup>24</sup> in discussing this subject, does not speak from his own personal operative experience, but from that of others, since he says "In my last series of more than 300 non-malignant cases I have not lost a patient and in recent years a temporarily unsatisfactory result has been extremely rare." Disappointments after gastro-enterostomy may not be the fault of the operation but of many other circumstances if things go wrong. The success or failure of an operation may be due not only to the procedure itself but also to its performance in cases which do not need it.

A. The operation has been performed in the absence of any organic lesion justifying it. This is by far the most frequent cause, and the conditions for which the operation has been needlessly performed are two:

(a) *In Functional Disorders of the Stomach.* He recalls that it is not so long since a patient with duodenal ulcer was told he was the victim of "acid gastritis" or "acid dyspepsia," "hyperchlorhydria" or "neuralgia of the stomach" all believed to be functional states. Many so-called functional diseases have an organic basis. There are, however, a number of difficult cases of functional trouble with atony of the stomach or prolapse of this and other abdominal organs. These cases may be difficult to treat medically but they are often made a great deal worse by a short-circuiting operation. In such cases further operative treatment should be reparation of the mistake of the too-enterprising predecessor. The anastomosis must be undone, and the stomach and intestines returned as far as possible to their original condition.

(b) *In Cases of Chronic Disease Elsewhere.* The original diagnosis of ulcer of the duodenum or stomach, should be verified after the abdomen is opened. Ulcer is always a visible, demonstrable, palpable lesion and if no ulcer is found, no operation should be performed. "The day is long past when a surgeon is entitled to accept a clinical diagnosis, no matter how confidently made, as a sufficient warrant for an operation." If no ulcer is found, search should be made elsewhere in the abdomen for a possible cause of the symptoms, and failure to observe this rule has resulted in the performance of gastro-enterostomy for conditions remote from the stomach. The operation has been performed for the following diseases:

1. *Chronic Appendicitis.* Years ago Moynihan described a condition "Appendix dyspepsia" in which symptoms closely resembling those due to gastric ulcer were caused by a chronic lesion in the appendix, and special attention was directed to the presence of hematemesis or melena in these cases. Bloody vomit is more common in other diseases than in gastric ulcer of which it is not a very common symptom and the occurrence of hematemesis should raise the suspicion not only of ulcer but also of chronic appendicitis, splenic anemia or cirrhosis of the liver.

2. *Tuberculous Disease of the Intestine.* Tuberculosis of the ileum, cecum, and ascending colon has been present in a small number of cases where gastro-enterostomy has been performed in the absence of gastric and duodenal ulcer. In England and in Scotland intestinal tuberculosis is by no means uncommon (impure milk supply). Since pyloric spasm, hyperacidity, pain and vomiting are occasionally present the mimicry to ulcer is apparent.

3. *Cholelithiasis or Carcinoma of the Gall-bladder.* Gall-stones declare their presence in all cases, except those in which a single cholesterol stone is present, by symptoms of dyspepsia and often of hyperchlorhydria. Many gall-stone cases are diagnosed gastric cases.

4. *Cirrhosis of the Liver.* There is often dyspepsia, flatulence, heaviness, soreness frequent eructations, loss of appetite, foul tongue. Hematemesis or melena or both may be profuse, but the absence of orderly development and precision in the time and character of the symptoms, makes the differential diagnosis between cirrhosis and ulcer rarely difficult.

5. *Splenic Anemia.* Moynihan has known gastro-enterostomy to be performed for this disease because of the hematemesis. In 2 cases he did a splenectomy.

6. *Tabes Dorsalis.* He has seen 5 cases operated upon, and there is no excuse for the mistake. The coincidence of ulcer and tabes is shown by one case who had tabes and duodenal ulcer, the latter demonstrated at the time of operation.

7. *Disseminated Sclerosis.* One case of Moynihan's had had a short-circuiting operation performed—the surgeon had found no ulcer, though the attack of pain and gastric distention suggested its probability.

8. *Vomiting of Pregnancy.* Two patients were operated upon, although, he says, vomiting is neither a common nor a serious symptom of ulcer.

9. *Lead Poisoning.* One patient was subjected to surgical treatment although no ulcer or scar was present. All signs of lead poisoning were definite.

10. *Prolapse of Kidney.*

11. *Colic Adhesions.* "Many patients who suffer from vague dyspepsias ascribed perhaps to intestinal stasis, or to chronic appendicitis, disclosed on the operation table this condition: A membranous band, broad above, where it takes origin from the posterior abdominal wall, the under surface of the liver, the pelvis of the gall-bladder, cystic duct and the duodenum, narrows below as it crosses the ascending colon to be lost on the peritoneum, to the inner side of the ascending colon, and on the enteric mesentery. Below this band which is quite different from a "Jackson's membrane" the cecum and the ascending colon are distended and soggy. Very often the appendix looks turgid, thick and stiff. Removal of the appendix, to which the troubles are ascribed, gives little or no relief. Division of the band allows adhesions to reform. The only practice likely to give good results is the removal of the terminal ileum, cecum and ascending colon. The performance of gastro-enterostomy, of course, makes matters worse."

12. *Epigastric Hernia*. The chief complaint is of indigestion, dragging, heaviness, etc.

B. *The Operation has been Incomplete*. It is better always to remove the appendix and to remove stones from the gall-bladder or drain it if there is any indication for these. Moynihan calls attention to the presence of subserous deposits of fat, especially near the pelvis and the cystic duct, which is the first sign visible from the exterior of an infection of the walls of the gall-bladder from within. The ulcer itself should be folded in and the first part of the duodenum covered over by the two omenta. Only by these means is perforation prevented. He rarely practices excision of the ulcer, exclusion of the pylorus, or partial duodenectomy and gastrectomy in duodenal ulcer. The infolding of the ulcer of course narrows the pylorus for a time but this soon recovers itself with the disappearance of the ulcer.

C. *Defects in Technic*. Under this heading, Moynihan writes at length but the reviewer believes it of greater interest to the surgeon than to the internist.

D. *Late complications* may develop after an operation performed in a case requiring it without any technical flaw.

1. *Jejunal Ulcer*. This is the most serious sequel. Although the causes are unknown it is probable that these contribute: the use of unabsorbed sutures, inaccurate apposition of mucous membrane, bruising of the part of the viscera embraced by clamps with result that a hematoma forms, a continuance of the cause of the original duodenal or gastric ulcer and a persisting hyperchlorhyria.

2. *Carcinomatous Change in a Chronic Gastric Ulcer*. If the ulcer is very large, burrowing deeply into the liver or the pancreas and near the cardiac end of the stomach, he performs gastro-enterostomy in  $\gamma$  and into the proximal limb of the jejunum below the duodenojejunal flexure, he introduces a tube, performing jejunostomy. Through this tube the patient is exclusively fed, for few or many months, until an x-ray examination suggests that the ulcer is healed.

*Symptoms after Unsuccessful Gastro-enterostomy. Pain.* Due to:

1. Revival of activity in an unhealed ulcer.
2. Pressure of a jejunal ulcer.
3. Adhesions crippling the proper action of the stomach or jejunum.
4. The presence of some other disease overlooked at the time of operation.

*Hemorrhage may be due to:*

1. Separation of a suture.
2. Continuing activity in a duodenal or gastric ulcer.
3. Jejunal ulcer.
4. Presence of some other disease as enumerated above.

*Vomiting may be due to:*

1. Obstruction due to defects in technic.
2. Functional cause.

*Diarrhea may be due to:*

1. Too rapid emptying of the stomach.



2. Some pathologic lesion in the intestine which has been overlooked.
3. Offensive character of the escaping contents.

The final word in diagnosis is the x-ray, but no matter what the diagnosis no clinical signs or clinical opinion can stand against the conditions revealed to hand and eye at the time of operation.

Another paper along the same line of thought is by Sherren<sup>25</sup> to the effect that useless gastro-enterostomies are being performed, which accounts for much of the continued ill health after operation. Sherren's article is mostly from the surgical point of view and deals with the technical side of the question, namely, such things as—whether it is wise to practice pyloric exclusion, the proper suture material, the location of choice in placing the gastrojejunal opening and many things of the same nature. The main conclusion which Sherren derives from a careful study of his numerous cases is that gastrojejunostomy for chronic gastric ulcer will become a less frequent operation and that partial gastrectomy will succeed it as the operation of choice.

**GASTRIC ULCER TREATED BY NERVE BLOCKING.** Inspired by the operation devised by Alvarez, of Spain (bilateral avulsion of the fifth, sixth, seventh, eighth and ninth intercostal nerves), Parker<sup>26</sup> has tried the well-known nerve blocking technic as employed in trifacial neuralgia. "A preliminary hypodermic of a quarter of a grain of morphin is given fifteen minutes before operation. The patient, sitting in a chair, leans forward over the table with arms fully extended above the head. The operation field is prepared in the usual manner. A long, strong hypodermic needle is inserted between the ribs about one and a half inches from the spine and is pushed forward until the resisting intercostal muscles are reached. Continuing a little beyond this resistance the nerve may easily be located, contact with the needle causing characteristic pain. About  $\frac{1}{2}$  c.c. of one-tenth of 1 per cent. cocaine solution is injected. After a few minutes the first syringe is removed leaving the needle in place. A second containing 5 to 10 c.c. of 60 per cent. alcohol is attached and the contained solution injected freely into and around the nerve. All ten nerves are similarly located. As the nerves are infiltrated, the patients describe their sensations, which vary greatly, the sixth giving in practically all cases their typical ulcer symptoms. A short time after the injections numbness is complained of in the abdominal wall and back. The following day an analysis of the gastric contents shows a reduction in free hydrochloric acid and total acidity." Parker has treated fourteen patients by intercostal nerve blocking, and reports satisfactory results.

The method of Alvarez mentioned by Parker was described some years ago, but there is an abstract in the *Journal of the American Medical Association*, 1919, lxxiii, 1481, which is apropos of Parker's paper.

**INDIRECT SURGICAL TREATMENT OF GASTRIC ULCER.** Alvarez<sup>27</sup> explains certain cases of gastric ulcer as the result of the excessive action of the sympathetic nerve innervating the stomach. This nerve has both

<sup>25</sup> Lancet, March 27, 1920, p. 69.

<sup>26</sup> New York Medical Journal, 1920, cxi, 418.

<sup>27</sup> Abstract, Journal of the American Medical Association, 1919, lxxiii, 1481.

a sensory and secretion-promoting function, and likewise a vasoconstricting action. When functioning to excess, there inevitably follow hyperchlorhydria and hypersecretion at the same time as anemia of the mucosa. The vasoconstricting influence deprives the mucosa of its proper nourishment and leaves it defenseless against the extra corroding action of the hyperchlorhydria which acts on the mucosa abnormally long on account of the hypersecretion. A further factor is the spastic closure of the pylorus from the irritation induced by the hyperchlorhydria. The whole train of phenomena can thus be traced to the excessive functioning of the sympathetic, and this he attacks by stretching the nerve involved to induce, as he says, "*conmocion a distancia del gran simpatico toracico*." He has thus treated 53 patients and reports 25 completely cured and 8 improved. The outcome is not known in 10 cases and no benefit followed in 10 others. In the cases of failure, organic stenosis of the pylorus was evidently a factor, and this contraindicates this method, he says. He describes the technic and gives the details of a number of typical cases. Lately he has been restricting the intervention to stretching the fifth intercostal nerve on both sides. At first he acted on the sixth, seventh, eighth and ninth. The nerves are severed and each is stretched with forceps aiming to act on the great sympathetic and the semi-ganglia and through them on the nerve fibers passing directly to the stomach. The consequence is an immediate vasodilation with hyperemia of the gastric mucosa, suppression of the hyperesthesia and hypersecretion, and as the consequence of this, arrest of the tendency to spastic contracture of the pylorus, and hence normal evacuation of the stomach contents.

Urrutia<sup>28</sup> insists that international statistics show that ample resection of the stomach does not have a much higher death-rate than simple gastro-enterostomy while the results are incomparably better. In a recent series of 82 cases of resection the mortality was 4.8 per cent., these patients succumbing to acute dilatation of the stomach, pneumonia, paralytic ileus or chloroform jaundice. In a previous series of 117 cases the mortality was 6.6 per cent., while it was 6 per cent. in 115 gastro-enterostomy cases. He mentions Alvarez's proposal to treat gastric ulcer by stretching the fifth, sixth, and seventh intercostal nerves on both sides and resecting the fifth. This may be useful with rebellious hyperchlorhydria, but seems irrational for an already established hard ulcer.

Gallart and Ribas say that the cicatricial changes found in the pylorus and elsewhere in the stomach testify that gastric ulcers can and sometime do heal spontaneously. They applied Alvarez's nerve stretching technic in 2 cases, but are unable to pass a decisive judgment on it. In only 8 per cent. of their gastric ulcer cases were conditions favorable for an operation; in all the others there were adhesions, multiple ulcers in 12 per cent., and extensive and intense gastritis was the rule. They state that the mortality from resection is from 20 to 30 per cent. in general, while gastro-enterostomy has a death-rate of only 3 or 4 per cent.

<sup>28</sup> Abstract, Journal of the American Medical Association, 1920 Lxxiv, 923.



and definite results are realized in 65 per cent. of the cases. In 2 of their cases cancer developed later. When there were disturbances they were almost always from closing up of the new opening, or from peritoneal bands, or adhesion to the pancreas, or irreparable lesions of the gastric glands. Pelaez's mortality in 128 gastro-enterostomy cases was direct in 2.14 per cent., total, 11.42 per cent. In 37 of his 140 peptic ulcer cases, the lesion was in the duodenum.

**Hour-glass Stomach (Bilocular Stomach).** Biloculation of the stomach exists when that organ is constricted in the middle and assumes an hour-glass shape. It is thus divided into two pouches: the one superior or cardiac, the other inferior or pyloric, the two pouches communicating by an orifice or canal.<sup>29</sup>

The biloculation may be temporary or permanent. (a) *Temporary.* This is due to a spasm which constricts for a moment the stomach in its middle portion. (b) *Permanent.* This may be due to an extrinsic cause; that is to say, compression by a large liver, spleen, or distended colon; it may be due to a permanent spasm which arises at the site of an evolving ulcer; it may be due to the cicatrix of an ulcer on the lesser curvature.

**ETIOLOGY.** True biloculation is due to a mediogastric stenosis which is in turn caused by the cicatrization of a gastric ulcer. The ulceration itself may be produced by caustics, syphilis, and tuberculosis, but 98 times out of a 100 it is the consequence of a simple ulcer of the lesser curvature especially ulcer situated at the middle portion of the curvature, which it straddles (saddle ulcer). The ulcer can provoke the mediogastric stenosis in several ways:

1. By spasm or annular contraction of the musculature at the level of the ulcer, a notch is produced on the greater curvature opposite the ulcer of the lesser curvature.

2. By thickening or infiltration of the walls of the stomach. The ulcer becomes callous, and though inflammation or through perigastritis, adhesions are formed, subserous thickening and finally cancerous degeneration which through its rigid character immobilizes the portion of the stomach lying between the two contractile and supple segments.

3. By cicatrization of the ulcer and fibrous retraction of the cicatrix, a retraction which involves the submucosa and muscularis mucosæ.

Pauchet has operated in 19 cases of mediogastric stenosis not due to cancer. Three times there was "cure" of the ulcer (an annular cicatrix); seven times there was a non-cicatricial callous ulcer, nine times perforating ulcer, penetrating into the liver, pancreas, abdominal wall.

**PATHOLOGIC ANATOMY.** 1. *Narrowing.* This corresponds generally to the middle portion of the lesser curvature where the ulcer is usually located (in 20 cases of gastric ulcer, 19 were found to be on the lesser curvature). The so-called "pyloric" ulcers are either duodenal or in the lesser curvature near the pylorus, but their original site is the lesser curvature. The constriction is rarely annular, there being nearly always a zone of healthy mucosa at the level of the greater curvature, a zone

<sup>29</sup> Pauchet: Presse médicale, July 24, 1919.



which may be nevertheless quite narrow. The narrowed portion of the stomach has usually the shape of an incomplete ring, the circle being broken at the level of the greater curvature. It is generally several centimeters in length, and the canal is eccentric in the neighborhood of the lesser curvature. From the peritoneal side the stenosis is seen as a scar, which may be hidden or not beneath perigastric lesions. In the majority of cases, Pauchet has found a burrowing ulcer penetrating the pancreas, the liver, or even the anterior abdominal wall, sometimes two or three organs at the same time. Upon opening the stomach, there will be seen a complete lower pouch, and a narrow ring arising from the upper pouch. This ring is joined to the lower pouch by a narrow band of healthy gastric tissue belonging to the greater curvature. The stenosis, if the facts are to be stated correctly, does not exist, but the area between the two pouches is made up of organs corroded by the ulcer. In the majority of cases, the narrowing is not composed of a true cicatrix, but by evolving callous penetrating ulcer.

2. *Cardiac Pouch.* The upper portion of the hour-glass stomach is generally the larger, equaling or exceeding the volume of the normal stomach. It is large because (a) a stenosing ulcer of the lesser curvature is nearer the pylorus than it is the cardia, (b) alimentary stasis. The distention may be associated either with thickening or thinning of the walls. If the upper pouch is situated high, the summit may fill the concavity of the diaphragm above the cardia, if it is low, the greater curvature falls, becomes a dilated *cul-de-sac*, is shoved to the right and thereby increases the stenosis. Pauchet has found occasionally that the cardiac portion is of the same size as the pyloric pouch, but in these instances the constriction has been high.

3. *Pyloric Pouch.* Although, as has been stated, it is generally smaller than the cardiac pouch, it is found at times to be larger, this being the case when there is a coexisting duodenal stenosis.

COMPLICATIONS. Of the following complications, the author has encountered but the first five:

1. Mediogastric stenosis together with duodenal stenosis.
2. Stenosis accompanying a perforating ulcer penetrating the abdominal wall, liver or pancreas.
3. Carcinomatous degeneration of a stenosing mediogastric ulcer.
4. Perigastric pus formation.
5. Gastrocolic fistula corresponding to the place of constriction.
6. Volvulus of the pyloric portion.
7. Acute occlusion of the mediogastric canal.

SYMPTOMATOLOGY. I. The classical syndrome (vomiting, pain, hemorrhage) is rare; gastric or duodenal ulcer exhibits painful phenomena of gastritis, hyperacidity, acid regurgitation, the symptoms being aggravated by food, and relieved by bismuth. Remissions are seen, simulating cure but these are followed by periods of recrudescence. The longer the disease exists, the shorter are the remissions of "health," the more painful are the symptoms. The majority of the cases lead an ordinary life and are thought to be "dyspeptics, neurotics or neurasthenics."

II. *Painful Phenomena.* These are not due to mediogastric constrictions but are caused by the chronic ulcer producing the stenosis. The ulcer is often penetrating and in this case the pain is accentuated. Often the pain is present all day, appearing after breakfast and being increased after the taking of any food. Epigastric and dorsal pain is common and often is a sign of a perforating ulcer of the lesser curvature. Vomiting does not stop the pain but dieting and rest alleviate it somewhat.

III. *Vomiting* is the rule; if it is frequent it is due to ulcer not stenosis; if it occurs at intervals, regularly and copiously, it is due to stenosis and corresponds to the emptying of the cardiac pouch, but later it contains food (stasis) and differs in no way from that seen in pyloric stenosis.

IV. *General Condition.* It is bad, and emaciation, asthenia and anemia are all the result of stenosis, whether it be pyloric or mediogastric.

V. *Physical Signs.* (a) Inspection and palpation do not differentiate pyloric obstruction from mediogastric stenosis; distention, dilatation of the stomach and visible peristalsis appear at the time of the pain, as in pyloric stenosis.

(b) The stomach tube shows alimentary stasis but does not distinguish the cause.

(c) The stomach tube associated with lavage shows three phenomena which are of considerable diagnostic value:

1. The lavage water is recovered only in part because some of it has entered the pyloric pouch.

2. The liquid at first is returned clear, then suddenly a liquid containing food particles is recovered. These are from the pyloric pouch, the latter's contents being reflected back through the mediogastric canal.

3. The stomach is washed and well emptied by the tube, after which clapotage limited to the pyloric pouch is found which has not been emptied.

(d) *Inflation of the Stomach.* By this means it may be possible to make out two distinct sacs separated by a band of dulness. Or the cardiac pouch alone may fill and become tympanitic in the left hypochondrium, while the lower sac may be dull. This condition may change in a moment, so that the lower sac becomes distended and tympanitic, while at the same time the rush of air through the constriction may be heard as a gurgle, synchronous with breathing.

(e) *X-ray* gives the most valuable information. The examination, made twelve hours after an opaque meal, shows the stomach in the shape of a J, the upper portion being separated by a clear space from the barium below. Very little liquid is required to fill it in the vertical sense, and it dilates only in the vertical direction, while preserving its regular and normal caliber. The bilocular stomach, on the other hand, has a characteristic appearance; at times it is composed of two black parts joined together by a black, narrow band, the whole being placed on a quasi-vertical axis or a little oblique—low and to the right; at other times, there are two distinct shadows, the one above, and to the left, in the shape of a truncated cone or crescent, with its air bubble, the other below, and to the right, separated from the other by a lacuna. The

second pouch forms a segment of a circle, with the convexity below, and it has no air bubble (magenblase). The pyloric pouch shows a shadow several minutes after the cardiac pouch. Under digital pressure, the two sacs are movable, in respect to one another, there being no normal stomach shadow when the lower portion is raised. It is impossible to empty the cardiac pouch into the pyloric pouch and it is equally impossible to cause the contents of the latter to enter the upper sac.

*X-ray Studies of the Bilocular Stomach.* In the *Archives des Maladies de l'appareil Digestif*, is an abstract of an Italian paper by Sessa, the original, being according to the abstractor, a very important and comprehensive contribution. After reviewing hastily the functional causes of biloculation (atony, neurosis, spasm) which may lead to diagnostic errors, Sessa discusses organic causes (ulcer, cancer, syphilis) and gives in detail the signs which distinguish the two most important groups: (1) Biloculation from ulceration (almost always ulceration of the lesser curvature accompanied sometimes by juxtapyloric ulcer) and (2) biloculation from cancer.

#### 1. *Biloculation Due to Ulcer.*

(a) Increase in the size of the stomach due to hyperchlorhydria, which causes gastric stasis because of closure of the pylorus, and because of the narrow passage between the two sacs.

(b) B-shape of the stomach—because of the rigidity of the lesser curvature (site of the ulcer) spasm is produced only on the opposite wall.

(c) The upper sac is shaped like a wallet.

(d) Lower sac being drawn toward the vertebral column by adhesions, is often on the same level as the upper sac.

(e) The channel between the two sacs is lateral in respect to the stomach and within on the lesser curvature. It is shorter than in cancer, and is straight and regular in appearance.

(f) In the case of perforating ulcer there is frequently a diverticulum in the region of the lesser curvature.

(g) Pain is elicited by palpation at the level of the stricture.

(h) In the case of an additional ulcer of the pylorus, Brûgel's sign is present: sharp contour, immobility of the superior border of the pylorus, which being rigid does not contract.

(i) The bismuth stops at the level of the channel then passes slowly into the lower sac (if there is a rapid passage of the opaque meal then there is also the appearance of spasm).

(j) Strong peristaltic and antiperistaltic movements.

#### 2. *Biloculation Due to Cancer.*

(a) No increase in the size of the stomach. Pyloric insufficiency due to hypochlorhydria.

(b) X-form of mediogastric constriction.

(c) Upper sac is funnel-shaped.

(d) The canal is central in reference to the stomach or situated outside on the greater curvature, long, rather large, irregular, indented.

(e) Simultaneous filling of the two sacs.

(f) Very feeble peristaltic movements due to rigidity of the walls.



**Gastric Cancer.** THE OPERABILITY OF GASTRIC CANCER AS DETERMINED BY THE ROENTGEN RAY. Carman<sup>30</sup> makes the following grouping according to the roentgen divisions of the stomach: Group 1—tumors of the pars pylorica, operable zone; Group 2—tumors of the pars media, the questionable or borderline zone; Group 3—tumors of the pars cardiaca, the definitely inoperable zone.

1. *Operable Tumors.* As approximately 70 per cent. of all gastric cancers occur at the pyloric end of the stomach, and as about 95 per cent of all lesions which encroach on the gastric lumen are carcinomatous,



FIG. 7 (263349).—Filling defect and obstruction due to tumor of the pyloric end of the stomach. The irregularity corresponds to a palpable mass. The lesion is operable "so far as the stomach is concerned."

a lesion in the pars pylorica should make one strongly suspicious of malignancy. Often cases which present such severe symptoms as to seem inoperable, prove operable on *x*-ray examination, for even a very large palpable tumor may be resected if it is confined to the lower half of the stomach. A palpable tumor does not prevent surgical intervention, but it does mean that the lesion has existed for a long time, and that metastasis may be present. The roentgen examination can pro-

<sup>30</sup> Journal of the American Medical Association, 1919, lxxiii, 1513.

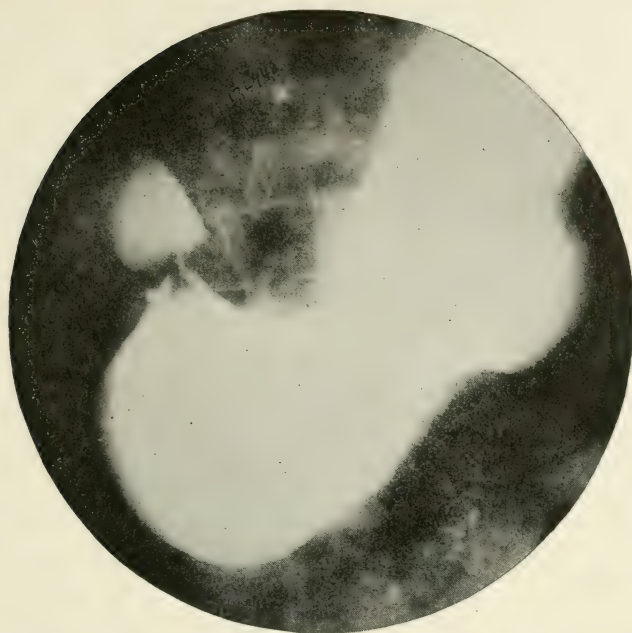


FIG. 8 (134942).—A small filling defect immediately prepyloric, with obstruction. No corresponding palpable mass. Lesion favorable for operation.



FIG. 9 (149635).—Filling defect with obstruction in the operable zone. The lesion was operable so far as the stomach was concerned, but proved to be inoperable because of metastasis found at operation.

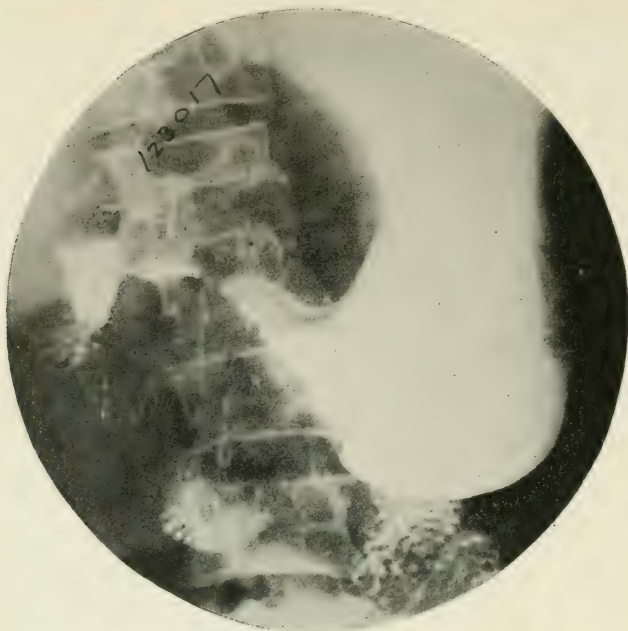


FIG. 10 (106837).—Gross filling defect extending into the questionable zone. Operability of tumors of this extent can be determined accurately only by an exploratory incision. The tumor was found to be inoperable because of posterior attachment.

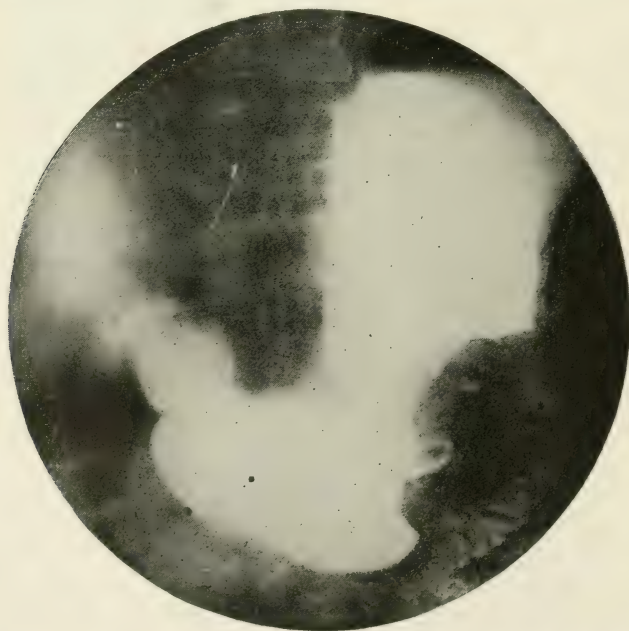


FIG. 11 (123017).—Filling defect of greater curvature involving the operable and questionable zones. Operability questionable so far as the stomach is concerned. Operation: sleeve resection.





FIG. 12 (109449).—Tumor involving questionable and inoperable zones. A tumor in this location is indisputably inoperable.



FIG. 13.—Tumor located in the inoperable zone. Operation is contra-indicated in cases of this type.

nounce on the operability of a tumor only with respect to the stomach, for it cannot discover metastases, except gross metastasis to the lungs and bones, which occurs so rarely as scarcely to merit discussion. The clinician can prevent useless operations in some cases believed by the x-ray to be operable by finding metastasis to the rectal shelf, supraclavicular glands, umbilicus and the skin.

2. *Borderline Cases.* Tumors of this group are those which extend so far up on the stomach wall that their resection is uncertain. Removal of these tumors depends on the skill and dexterity of the surgeon. The position and size of the stomach may be a surgical drawback, and Carman says if the roentgenologist is familiar with the operator's ability and technique, he can give a much better opinion. Tumors of the fundus which do not produce pyloric or cardiac obstruction, and which are not palpable because of their high location, may exist for a long time without causing much inconvenience, and by the time clinical diagnosis is definite they are usually inoperable. As free mobility of a cancerous stomach favors resectability, as fixation resulting from extension to adjacent organs makes successful intervention less probable, as cancer, roentgenographically demonstrated as small may at operation be found to have invaded or become adherent to adjacent abdominal organs, and as metastasis may exist without detection by the x-rays, the roentgenologist is so often forced to make a relative diagnosis of operability in the borderline group of cases that it might be called the exploratory group, for on the surgeon devolves the operative decision.

3. *Inoperable Tumors.* The tumors of this group are in the cardiac end or they have spread from a pyloric or fundal carcinoma to within the inoperable zone. The tumors in this region are easily recognized by the x-ray as inoperable.

LINITIS PLASTICA.<sup>31</sup> Smallness of the stomach (microgastria), thickening of the walls, rigidity of the cavity—these are three clinical and radio-scopic signs which are pathognomonic. Carnot describes three forms depending on the point of origin—either the wall or the orifices of the stomach: (1) Linitis plastica (*linitis gastrique*) without involvement of the orifices; (2) Linitis cardiogastrica; (3) Linitis gastropylorica.

1. *Linitis Gastrica without Involvement of the Orifices.* In such a case, with the three cardinal signs stated above, the motor functions of the stomach are annihilated in the affected zone but the orifices remaining unattacked, the pylorus can still functionate. As a result, after eating, the pylorus closes, and the food immediately enters the little gastric pouch and from there it enters the esophagus where it accumulates or whence it is ejected by vomiting. This form of linitis then shows a dysphagic syndrome simulating esophageal obstruction, the syndrome of pseudostenosis of the esophagus, called also the syndrome of Soupault. This syndrome is characterized by the following:

(a) There is difficulty in swallowing, especially provoked by solid food.

(b) In contrast to the symptoms of stenosis, there is the ease with which a sound or tube may be passed through the esophagus and cardia.

<sup>31</sup> Paris médical, 1919, ix, 481.

If one attempts to fill the stomach through the tube, there is a reflux of liquid along the wall of the tube; all attempts to inflate the stomach fail.

(c) Examination reveals, sometimes, a little hard rigid mass, situated high up in the epigastrium and not descending when standing, and having no gastric tympany or clapotage.

(d) The x-ray gives the exact diagnosis. The fasting stomach contains neither liquid nor gas, but on the contrary the walls are abnormally visible being very much thicker than in health. Often a double contour is seen conforming to the hypertrophy. With a barium meal there is an immediate epigastric shadow, small in dimensions, and situated high up. There is no sudden fall of the contrast meal to the bottom of the stomach, but the shadow is constantly high, gradually mounting higher and higher into the esophagus, which is seen to dilate little by little. Thus is formed a gastro-esophageal shadow, and with the dilated esophagus and retracted stomach the tube is seen as of one diameter.

(e) There is finally the syndrome of absence of gastric juice, absence of stasis, presence of inanition and progressive cachexia.

2. *Linitis Cardiogastrica*. In this second form the hypertrophic sclerosis is submucous and extends along the body of the stomach to the cardia and then to the inferior portion of the esophagus. Therefore, together with the reduction in the volume of the stomach, there is induration of the cardia with stenosis, or more commonly stenosis and incontinence. The clinical picture is one of dysphagia, regurgitation of mucus or of small portions of food. There exists, then, a *real cardio-esophageal stenosis*. The sound or tube will be stopped at the cardinal orifice or even above it (40 cm. from the teeth), and the diagnosis is inevitable, of a neoplastic stenosis of the esophagus. The x-ray recognizing, however, and the three cardinal signs should remove any uncertainty.

3. *Linitis Gastropylorica*. When there is extension of the process to the pylorus, the latter becomes rigid and incapable of contracting. The process may stop there, but not infrequently the duodenum is involved. In any case there is profound disturbance of gastric functioning (evacuation). There arises then incontinence of the pylorus. Should the induration of the pylorus be so extensive that the orifice is completely occluded, then pyloric stenosis results. Pyloric incontinence is the common result, however. Food (*l'estomac s'évacue d'emblée*) is simply chuted into the duodenum, and there is little tendency to esophageal reflex. X-rays show this "water spout" emptying very well, the shadow appearing in the esophagus, stomach, and duodenum simultaneously, while esophageal and gastric evacuation is retarded.

Carnot calls attention to the fact that this organic pyloric incontinence must be distinguished from the functional seen in cases of duodenal ulcer, and this can be done by instilling into the stomach hydrochloric acid which will, in the latter instance, provoke closure of the pylorus. The sham test-meal, quoted elsewhere in this monograph, is a useful means of provoking an acid pyloric secretion with a resulting pyloric closure.

An article on pyloric incontinence (*incontinence pyloriques*) or pyloric



insufficiency, by Udaondo, Cavulla and Gonalous<sup>32</sup> will be reviewed here in connection with Carnot's paper. Carnot quotes a case, the typical sign of which was a wide open pylorus which permitted the passage of the opaque meal, with no stopping at the pylorus, directly into the duodenum. The authors named above make a distinction between this condition, pyloric insufficiency, and premature emptying. Apropos of their case report, they review the literature somewhat at length. Although the clinical diagnosis has often been made, one can be sure in no case, without the aid of the *x*-ray. Several varieties of insufficiency have been described, functional as well as organic. The vast majority of the cases are of the latter class, and the cause is generally malignant, or of the linitis plastica types mentioned by Carnot. Bouveret has observed a form of pyloric cancer, in which, with the destruction of the muscle fibers, there was an auto-elimination of cancerous masses by necrosis, leaving an opening incapable of closure. Again when there is invasion of the walls of the stomach from a pyloric neoplasm the orifice is kept open due to rigidity of the walls of the stomach. It is in this type that Bard emphasizes the appearance of diarrhea with violent colicky pains. When cancer involves the median portion, insufficiency results from absence of the pyloric reflex (Carman) and evacuation from the stomach is rapid and complete, as is also the intestinal transit, so that in six hours the opaque meal is found in the descending colon. It is in this type that low acid values are seen, which hypo-acidity is held to be responsible for the deficient pyloric reflex.

Gastric syphilis with pyloric incontinence has simulated linitis plastica almost exactly and other non-malignant causes of the insufficiency are pyloric ulcer, pyloroduodenal adhesions, cicatricial stenosis of the duodenum, compression of the duodenum by a movable kidney, to mention a few of the conditions cited by Udaonda and his collaborators.

**Pyloritis.** Loeper<sup>33</sup> states that, of the various syndromes shown by gastric diseases, the pyloric syndrome is the most definite. It is, above all, characterized by late pain, that is, pain which does not appear until the end of the gastric cycle. It may be a pain of any variety, and it may radiate in any direction but it preserves its chief characteristic of appearing late. Since it is coincident with the evacuation of the stomach, it comes later if the meal has been copious, and it is more intense the more indigestible the meal has been. Some pyloric syndromes are transient, appearing one day and disappearing the next, in other cases they take the form of crises. Some appear suddenly, with no prodromal symptom; others are manifested gradually.

With the filling of the stomach, or shortly thereafter, contractions begin in the fundus and work toward the pylorus. The *x*-ray enables one to determine the point of origin, as one knows, on the greater curvature at the junction of the pars verticale and pars horizontale, and shows us that there is an interval of about twenty seconds between the contractions. Pyloric emptying begins in the first few minutes of diges-

<sup>32</sup> Arch. des mal. de l'app. dig., February, 1920.

<sup>33</sup> Progres médical, September 28, 1919.

tion, a little later when the stomach is atonic, a little slower when the pylorus is spastic. It continues until complete emptying of the organ, but it does not take place all at once, and emptying depends upon the character of the meal. There are substances which are immediately evacuated, there are others which are expelled only after a long sojourn in the stomach. Some are solids which need to be liquefied, others are liquids, and others are pasty masses; liquids leave first, solids last.

In the stomach the alimentary mass separates into two layers: the solid below, the liquid above. The liquid pours toward the pylorus and leaves early. It causes no pain, for in the majority of instances it is devoid of irritant action, and is therefore indifferent as far as the pylorus is concerned. Some substances require previous coagulation, after which they escape in clots, and leave early. During this time the solid mass is undergoing transformation into a more liquid form. According to the composition of the meal, this lasts from five to six hours; digestion of milk is more rapid than that of bread, that of raw eggs more rapid than of cooked eggs, cooked meat is digested more quickly than raw meat, fats more rapidly than starches. A complex meal is more difficult to digest than one that is homogeneous and is evacuated more slowly. It is when digestion is finished, toward the end of the second or third hour that the fundus begins to expel its contents and it is necessary for the pylorus to evacuate solid particles more or less perfectly digested. One can understand that for the pylorus this may be more or less difficult; moreover, there are certain substances formed during digestion which the stomach is unable to change further, and some of these are irritating to the pyloric isthmus.

It is at this moment that pain appears, being later if digestion is slower, intense if the mass is less homogeneous, and contains irritants above mentioned, more lasting if the mass is great. Therefore, pyloric pain is a pain of passage (*douleur de passage*) just as is the pain of gall-stones. It is certain that it is still more so, for the fundus contractions can of themselves cause pain if the pylorus is more resistant. This is the reason why a fibrous stenosis is painful, whereas the pylorus itself is really quite insensitive. In the pyloric syndrome there are then the passage through the pylorus and the fundus contraction. The first is due to a pyloric lesion and to spasm, the other is due to excessive effort of the organ struggling against a resistant orifice. Acidity plays a role as is well known.

The cause of the pain in the pyloric syndrome is always a defensive reaction, an obstacle, a resistance of the pylorus; it is sometimes only a reflex spasm and the causative factor may be elsewhere. Ulcer of the stomach is by far the most common cause of the syndrome, and the latter is justly said to be a symptom of ulcer. It is, however, probable that another lesion limited to the pylorus, and not ulcerative in nature, may produce the syndrome and this condition Loeper describes under the name gastritis of the pylorus or *pyloritis*.

Acute and chronic gastritis involves by preference certain parts of the stomach, and either the pylorus or fundus may be affected. Alcoholic gastritis, gastritis from gas or from infection is generally most pro-



nounced in the pylorus. The reasons for the pyloric localization are mechanical and anatomical. If the pylorus is an active organ, often irritated and fatigued, it is still more an organ with a special structure whose anatomy favors certain lesions. Its epithelial covering is made up of mucous elements; its glands are branched glands, and the basement structure is composed of two superimposed zones, the one dense, the other slack and loosely constructed. Its secretion is acid and mucus. Below the epithelium lies the muscle disposed in three layers, longitudinal, circular and oblique muscle fibers, and in them are the numerous nerve elements, fibers and ganglia, which form around the orifice the circle described by Openchowski and whose importance is nowhere else so great as in this locality. To these characteristics cellular, muscular and nervous, there is still another less well known, namely, development of lymphatic tissue in the mucosa of the pyloric region. In the stomach, lymphatic masses are infrequent, in the pylorus, they are extremely numerous. The pylorus is an organ rich in lymphatics and in this respect resembles the small intestine, and it is easy to comprehend how an inflamed pylorus can have its repercussion in the neighboring ganglia and can cause degeneration. Lymphangitis of the pylorus can in no wise be left out of consideration in discussing inflammatory processes and their dissemination, and the reaction of the pylorus is the greater since it is one of the sensitive zones of the pylorus with a highly developed nervous system. To that inflammation limited to the pylorus Loeper gives the name *pyloritis*.

In these cases, macroscopic examination is apparently negative but on section lesions are found about 1 cm. behind the pylorus. They consist of hypertrophy, destruction of the epithelial covering of the mucosa, tumefaction, swelling and edema of the gland cells. Between the glands there is leukocytic infiltration in an isolated area, consisting of polynuclear cells and eosinophils. At the base of the glands the lymphatic follicles are greatly hypertrophied, their outlines are irregular and lymphatic elements are scattered roundabout. In certain places, the swelling is so great that the follicles almost touch. Always they are delicately united by fibers running between the base of the glands and the muscularis mucosæ. Lymphocytes invade the spaces between the glands, filling these interstices and escaping by penetration of the epithelium. The submucosa is swollen and contains areas of congestion, with edema, and most notably lymph passages. The muscle is almost always intact but in some places lymphocytes are seen.

The symptomatology of any gastritis consists of pain, vomiting and alterations in gastric chemistry. It is especially upon the late appearance of the pain that the diagnosis rests. If, in a case of gastritis, diffuse though it may appear, the pyloric syndrome appears, then pyloritis is present. There is nothing to prevent one from saying that the syndrome is seen in ulcer, but in this case, the true diagnosis should be made. The gradual fading of the symptoms and especially of the pain, the amelioration of the syndrome by an appropriate regimen, the absence of true crises are elements of interest in the diagnosis. In other cases recourse must be had to the laboratory. The x-ray shows no profound lesion of



the pylorus, only a certain delay in the evacuation of the gastric contents, with no marked retention. Examination of the gastric juice and of the feces shows no blood. Hyperacidity may be present, but certainly it is less commonly found than in ulcer.

Cytologically, pyloritis is distinguished from certain forms of gastritis by the appearance after lavage of little round cells. These may be of two types: the one having a little nucleus, with the protoplasm homogeneous and staining strongly with eosin; the other having a large nucleus rich in chromatin and with a violet-colored protoplasm much reduced in amount. The first are lymphocytes and nowhere does one see them so abundantly as in inflammatory lesion of the pylorus. The last-named are pyloric epithelial cells, whose protoplasm has been contracted by action of the gastric juice. They are not easy to differentiate and neither the one or the other type of cell is pathognomonic, but the richness of the lavage water in round cells is an index of pyloric involvement.

In conclusion, pyloritis may be recognized by

1. The pyloric syndrome.
2. The presence of round cells after lavage.

It is distinguished from ulcer by the absence of blood. It is differentiated from diffuse gastritis by the absence or rarity of the large fundus cells. It is characterized anatomically by mucous lesions of the pylorus, and by lesions of the lymphatic system. One should not make a diagnosis of ulcer alone on the presence of late pain, one should not think of pylorospasm when cytologic examination shows inflammation to be present. A large number of pyloric reactions are not due to dyspepsia, but to inflammation of the pylorus. It is not impossible that pyloritis may be an early stage of erosion or ulcer.

The diet of pyloritis should be pure milk, or milk with sodium citrate which by preventing coagulation decreases the difficulty of passing through the pylorus. Alkalines, fasting or three hours after eating are useful. Citrated alkaline solutions are valuable, acting as a lavage when given before the meal. Bismuth is especially useful.

**Achylia Gastrica.** This condition, or, as Bassler<sup>34</sup> prefers to call it, "Gastric Cell Primary Atrophy" may be divided into (1) Those in which it is normal in the individual and has not, and will not cause symptoms; (2) the psychologic cases; (3) reduced state of general body from fevers and senile condition; (4) endocrinitic or hormone disturbances of which we know little; (5) pathologic conditions of the stomach glandularis in which the secreting ability is destroyed by disease of the essential elements; namely, the acid and central cells. The last-named should be designated atrophic gastritis rather than achylia gastrica, the latter term properly being applied to the normal non-acid stomachs (which for some reason have acquired symptoms) to the psychologic endocrine, the general vitality reduction, and the senile cases. According to Bassler, almost every instance of so-called gastrogenic diarrhea with persistent achylia, whether increased amounts of mucus are present

<sup>34</sup> Journal of the American Medical Association, 1919, lxxiii, 405.

in the stomach or not, should be viewed most probably as an atrophic gastritis.

Studies made on the cadaver suggest that infections of long standing in the body cause a degeneration of gastric secreting cells through toxins, or from direct action of the bacteria in the stomach. Clinically, 40 cases were carefully studied, and, of these, 36 were found to have infections, while in 4 no form was discovered. Ten were head cases, and of these, only pyogenic sinus conditions, badly diseased tonsils and distinct pyorrhea were considered significant. Chronic middle ear conditions and tooth apex infections were not included unless one or more of the former mentioned conditions existed also. The 9 chest cases were all tubercular, 8 of the abdomen and pelvis (17), the gall-bladder, appendix, colon, renal female pelvic organs and prostate disease made up the group.

Bacterial examination of test-meals were made. In the simple, anachlorhydric cases, more bacteria of the fermentative kinds were encountered, and in the non-infective and non-atrophic cases, they were not pathogenic in kinds. In atrophic gastritis and the senile cases, the content was higher and tended to Gram-negative pictures in which the staphylococcus, streptococcus and streptobacillus, often actively mobile occurred as distinctive findings. Bassler has tried the effect of vaccines made from test-meals, but without success. As far as treatment is concerned, gastric lavage with lacto-farinaceous diet and alkalies and pancreas preparations seem to be as efficacious as any although in no case was there any return of normal acid or pro-enzymes.

Russell<sup>35</sup> believes the condition is much more infrequent than hyperchlorhydria, an opinion that will be shared by the majority of those who see numbers of gastric cases. He believes too, that the result of treatment is more dramatic than in the hyperacid cases, an opinion which I, personally do not share, and which is not shared, I believe, by the majority of gastro-enterologists. No matter the point of view one adopts with regard to Russell's paper, it contains some suggestions which are well worth presentation to the readers of this monograph.

The symptoms begin with a feeling of heaviness or load in the stomach, not a pain, but a discomfort. Later, there is a feeling of distention in the stomach and "due evidently to accumulation of air or gas," the eructation of which gives temporary relief. The discomfort comes on soon after food, but in some cases it is delayed, and it may, when once it discloses itself, last for hours, and the sense of oppression may be dissipated only by vomiting. The tongue becomes furred, the appetite is impaired and the bowels irregular, and usually constipated. There may be vomiting after every meal. The writer then details some cases, of little value, but says a noteworthy thing when he says "milk is one of the outstanding foods which perturb the meagre secreter."

Russell advises proper diet and medication but all he tells us is, that in 1 case he stopped the milk, gave farinaceous puddings with stewed fruit, all kinds of minced flesh, well seasoned, and acid and strychnin. How often have many of us tried just such a scheme, and how frequently

<sup>35</sup> British Medical Journal, December 13, 1919, p. 769.



have we found improvement! Hypochlorhydria is the most refractory of all gastric conditions, and I confess I have seen no dramatic cures such as one daily observes with hyperchlorhydria.

**TREATMENT WITH HYDROCHLORIC ACID.** Bie<sup>36</sup> reports a case of gastric achylia with enteritis and anemia for many years, refractory to all treatment. The patient was a physician of thirty-four, and Bie treated him with hydrochloric acid in doses large enough to supply the proper proportion for normal digestion. He gave at first 1 c.c. in 250 c.c. of water once a day, increasing this gradually to 5 c.c. in 250 c.c. of water and keeping up this dose at intervals for nearly three months. The acid was administered through a stomach-tube, 6 mm. in diameter. The effect on the enteritis was prompt and decisive, and by the fourth month the patient had recovered his strength and was able to resume his practice. There was no doubt that the cure of the enteritis and the anemia was the result of the hydrochloric acid treatment administered in doses larger than are usually given. In conclusion, Bie remarks that the advantage of kefir treatment in pernicious anemia may be due to the lactic acid in it which supplies the lacking acid in the stomach to a certain extent. It might be feasible to give hydrochloric acid with it. This treatment is not suited, of course, for all cases of gastric achylia, just as kefir has not always a favorable action in pernicious anemia. It might be advisable to give it a trial at least in every case. The hydrochloric acid was not given every day, only nine times in the first month and six times in the second month, the doses ranging from 1 to 8 c.c. of the acid in from 250 to 500 c.c. of water. The aim was to provide the acid in the same amount and fluid contents as in the natural reaction. The stomach secretes a 4 or 5 per thousand solution of the acid which corresponds to a dilution of the hydrochloric acid of the pharmacy of about 1 to 50. The acid was given fasting once a day.

**GASTRITIS (PHLEGMONOUS).** Sundberg<sup>37</sup> gives the details of 17 cases from the clinics at Stockholm and Upsala, and tabulates these and others he has found on record, a total of 215 cases of phlegmonous gastritis. His tabulation alone fills 60 pages, and his bibliographic references 8 pages. The inflammatory process develops mainly in the submucosa. He says that Hedenius was the first to suggest the infectious origin (1871); streptococci have been demonstrated in 71 of 95 cases examined. In only 8 per cent. of all the cases listed were the patients of the well-to-do class; 25 per cent. of the total number had been hard drinkers. In the 17 personally observed cases, there was always a history of chronic gastritis, and the secretion of gastric juice was abnormally low. The inflamed mucosa is peculiarly vulnerable, and the deficient gastric secretion leaves it defenseless. Infection can occur by direct implantation of germs or by way of the blood. Pus in the vomit is the most instructive sign of the affection, especially when the amount is large and the intervals short. Another instructive sign is that the pains which may come to resemble those of a perforating gastric ulcer subside when the patient sits up after reclining. This was constant in

<sup>36</sup> Abstract, Journal of the American Medical Association, 1919, lxxiii, 136.

<sup>37</sup> Ibid., 1919, lxxiii, 802.



his cases, and the high fever also testified against perforating gastric ulcer. In 33 per cent. of the fatal cases nothing was found to indicate peritonitis. Rational treatment can be only by resection of the diseased portion, but spontaneous recoveries are known. Cases in which after an exploratory incision revealing supposedly incurable cancers, the patients survived for years afterward, may have been cases of phlegmonous gastritis on the road to healing. The death-rate in his non-operative series was 92 per cent. Cases in men are nearly three times more numerous than in women. The ages were between twenty and sixty. High fever and general malaise, headache and thirst, with vomiting and sometimes violent and persisting hiccup often usher in the disease.

**Gastric Syphilis.** The first cases were reported by Andral in 1838, and thanks to the classical studies of Fournier, Hayem, Dieulafoy, and of Pater, gastric syphilis today is quite well known, and it is becoming more and more rare the oftener one considers it among his diagnoses. So writes Ramond.<sup>38</sup> In the large majority of cases violent hematemesis is the most conspicuous symptom, and ulcer of the stomach is the diagnosis generally made. In ulcerative gastric syphilis there may be the characteristic triad of Cruveilhier—pain, vomiting, hematemesis, so that suspicion is directed still more in the direction of ulcer.

Another form is that simulating chronic gastritis, with vomiting, pain, loss of appetite, but with no hemorrhage. Ramond quotes the case of Andreal which is the first ever published. A young woman, aged twenty-seven years, had suffered for two years, with vomiting, pain, and loss of appetite. Despite all that was being done for her, she became very much worse, and the attending physicians had despaired of her recovery, when four months later she complained of her throat, and upon examination there was found on the posterior wall of the pharynx an ulceration which had all the appearance of being specific. Andreal, despite the negative history, recognized the ulcer and, after considerable deliberation, administered bichloride of mercury in pill form, together with inunctions. It was a veritable resurrection! "After the twelfth inunction the condition of the patient was no longer recognizable as the same, vomiting had ceased, food could be taken without discomfort, the epigastric region was soft and not tender, and soon the patient recovered the plenitude of her health."

Gastric syphilis can simulate cancer, and Ramond quotes a case of tumor formation in Fournier's experience which resembled malignancy in practically every particular. It will be seen from Ramond's very conversational-in-tone, and therefore interesting paper that gastric syphilis is by no means a disease of uniform symptomatology, and all writers have agreed upon this. The true diagnosis is made by the results of treatment, but suspicion should be directed in the way of the true diagnosis by the finding of lesions in the skin, viscera, nervous system, scars of old lesions and by the Wassermann reaction. Treatment may be arsenical, mercurial or iodic (?), but especially mercurial. Many cases are cured by potassium iodide alone, and it is remarkable to note

<sup>38</sup> *Le Progres médical*, 1920, p. 7.

how well the stomach bears the iodides and salts of mercury. All ways of administering antisyphilitic treatment should be employed.

Haas<sup>39</sup> begins his report of a case of syphilitic tumor of the stomach by quoting Chiari, as finding but 2 cases in 243 syphilitic cadavers, and therefore believing the condition to be a rare one. According to Bensaupe, the reason so few are found at autopsy is because so many have been cured or prevented by antisyphilitic treatment. This patient of Haas was operated upon, but nothing was done since the surgeon found too great involvement of the stomach, with general metastasis, and closed the abdomen in the belief that the case was carcinomatous. Following the operation the patient's condition was much worse, and Haas finally decided upon the administration of salicylate of mercury and sodium iodide. Rapid improvement followed this treatment and at last accounts the patient was well and had performed well his duties in the war.

**Sarcoma of the Stomach.** Apropos of a case of gastric sarcoma, Loeper<sup>40</sup> has written an extensive article on the subject. The first account was written by Virchow in 1865, and since then there have been numerous publications, reporting large numbers; thus, Fenwick reports 50 cases, Lecène and Petit, 57, and Burgaud, 90. According to Lecène and Petit, the disease is more common in woman, affecting individuals between forty and sixty years of age. Although there has been some discussion as to whether many gastric carcinomata are not really sarcomatous in nature, Loeper feels that the disease is comparatively rare and he places the percentage of sarcomata occurring in the stomach as two.

Sarcoma of the stomach is always a tumor, and those afflicted seek advice about a hepatic or splenic tumor, or an abdominal tumor of some abdominal viscera. In many cases the diagnosis is not suspected and the true nature of the tumor is not revealed until operation. In two-thirds of the cases, tumor formation is preceded either by functional or general symptoms—anemia, dyspeptic symptoms which one is not able correctly to label, pain more or less definite, more or less localized, gastric or abdominal in nature, either critical or continuous; in other cases there is constant irritability of the stomach with frequent vomiting. It is because of the polymorphism of the symptomatology that Burgaud has seen fit to separate the sarcomata into two forms: the *endogastric* which provoke, in the majority of the cases, digestive symptoms, and *exogastric* which only rarely produce true gastric symptoms.

There are four symptoms by which a mature sarcoma is characterized: pain, vomiting, tumor and systemic disturbances. The *pains* are rather vague, and may be described as merely a sensation of discomfort, either intercostal or vertebral, or they may be very distinct in their expression. Occasionally, distress is concurrent with the digestive cycle, and pain means a sarcoma in the median or pyloric portion of the stomach. *Vomitus* is not constant, occurring in about 10 per cent. of the cases. Like pain, it may occur early or may not be seen until the condition is

<sup>39</sup> Arch. f. Verd. Kr., 1920, xxvi, 68.

<sup>40</sup> Progres médical, November 15, 1919, p. 455.



far advanced; vomiting then assumes the character of residual vomiting, the vomitus containing food eaten the night before. *Hematemesis* is generally slight and the blood is black, and although in a single case it may occur frequently, it is not a common sign in the majority of the cases. *Melena* is seen and may be present in the absence of hematemesis.

The *tumor* is hard, most often epigastric, sometimes subumbilical, frequently splenic or hepatic in its location. It is large and rounded like a cyst or abscess, and very frequently nodulated. There is but little tenderness, and the tumor is freely movable with respiration or on palpation. Tumor is rarely absent, but it may not be detected if it is distinctly pyloric. Dilatation and clapotage, together with the recovery of large amounts of liquid on aspiration, help in deciding that there is a tumor in the pyloric region or at least an obstruction. However, the stomach does not become dilated in every case, in fact the organ may become reduced in size. *Emaciation* and *anemia* are general signs. There is generally a leukocytosis (13-18,000) but there is nothing typical in the differential count.

Five forms of gastric sarcoma have been described: (1) abdominal; (2) anemic, resembling pernicious anemia; (3) dyspeptic; (4) a form resembling simple cancer; (5) peritoneal resembling bacillary peritonitis. The diagnosis is rarely made for the majority of the cases are confounded with cysts of the spleen, mesentery, ovary, and with abscess of the liver. The peritoneal form is often mistaken for tuberculous peritonitis, a mistake which is made more easy by the presence of fever. The dyspeptic form is usually diagnosed as carcinomatous stenosis, a diagnosis, substantiated by the x-ray which in no way helps one to recognize the true nature of the tumor.

In deciding between a sarcoma and an epithelioma, the age of the patient is a factor of assistance, for as a rule sarcomata are seen more frequently in young individuals. A very large tumor, and one which grows very rapidly speaks for sarcoma, whereas a tumor with grave cachexia is rather to be considered as epitheliomatous in nature. Enlarged glands in the supraclavicular fossæ are seen especially in cancer, but how rarely does one find this enlargement? Loeper says there is only one sure means of recognizing the condition and that is cytology. Examination of the stomach washings may reveal evidence of great value. In Loeper's case a large number of round cells were found which he believed to be lymphocytes, but which he confesses he should have recognized as sarcomatous in nature.

It goes without saying that the treatment is surgical. The results have been good. He quotes 22 operations; 14 of the patients were alive from three months to three years after laparotomy. Kimpton<sup>41</sup> reports a case six years after operation, and Frazier (quoted by Kimpton) cites a case of apparent health, fourteen years after surgical intervention.

## DUODENUM.

An important physiologic fact brought to our attention within the past year or two is that the duodenum is not essential to life,

<sup>41</sup> Boston Medical and Surgical Journal, 1919, clxxxi, 731.



that animals can live, thrive and remain healthy despite duodenectomy.<sup>42</sup> The latter authors verify the conclusions of Moorhead and Landes and extended the researches from the dog, to cat, hog, goat and monkey with a view to determining the effect of the operation on other species, particularly on the herbivorous and omnivorous animals. The animals remained in good condition, examination of the blood showed it to be normal with regard to cell counts, hemoglobin, carbon dioxide combining power and hydrogen ion concentration. The roentgen ray showed the course of a standard barium meal to be practically the same as in a normal dog. Experiments on the other species have been too recent to allow conclusions to be drawn, but it would seem that the removal of the duodenum in the hog is as innocuous as its removal in the dog. No data have been secured to show that the duodenum is of great importance in any of the species used.

**Carcinoma of the Duodenum.** Deaver and Ravdin<sup>43</sup> report a case of duodenal cancer and give a good summary of other cases of this infrequent disease.

The summary as given by Deaver and Radvin is:

1. Carcinoma of the duodenum is a rare condition. It is found in 0.033 per cent. of hospital autopsies.
2. The percentage of carcinomas of the entire intestinal tract originating in the small intestine varies from 2.5 per cent. to 3.1 per cent.
3. The relative proportion between carcinoma of the duodenum to that of the jejunum and ileum is 47.7 per cent. to 52.2 per cent.
4. Inch for inch the duodenum is much more liable to undergo carcinomatous change than the jejunum or ileum.
5. The relative frequency at various sites of duodenal carcinoma is as follows: First portion, 22.15 per cent.; second portion, 65.82 per cent.; third portion, 12.02 per cent.
6. Carcinomatous degeneration of chronic duodenal ulcers is not nearly so frequent as in chronic gastric ulcers.

## APPENDIX.

**Appendicitis.** In contrast to the preceding years, medical literature, I mean French and German literature, is full of articles on appendicitis. These articles deal for the most part with a stale, flat and unprofitable discussion of certain aspects of this condition which to us in America have long since become indisputable doctrines of common knowledge and universal acceptance. Just why the foreign physicians, especially the Germans, should write on such a subject as "Operative Indication in Appendicitis," as if it were a matter still of debate, is difficult to say, but, in general, most of the literature deals with questions answered by the American profession twenty years ago.

**ETIOLOGY OF APPENDICITIS.** Riff<sup>44</sup> makes a strong plea for the oxyuris as an etiologic factor in appendicitis. The oxyuris is essentially

<sup>42</sup> Moorhead and Landes: *Journal of the American Medical Association*, 1919, lxxii, 1127. Mann and Kawamura: *Ibid.*, 1920, lxxiii, 878.

<sup>43</sup> *American Journal of the Medical Sciences*, 1920, clxx, 469.

<sup>44</sup> *Presse médicale*, September 18, 1919, p. 521.

a family disease being transmitted from generation to generation, principally in bed. Almost all infested with the parasite complain of digestive disturbances, abdominal discomfort, alternating diarrhea and constipation, acute pains, with or without, elevation of temperature, coated tongue and bad breath. Such a person generally has a tender point in the right iliac fossa, and generally when the diagnosis of appendicitis is suspected one will be able to find the oxyuris or its eggs. The worm can produce typical appendiceal lesions, and often it can be discovered in the appendix itself. If the parasite finds enough food in the intestinal tract it will not attack the mucosa and this explains why for many months and even years it may inhabit the gut canal and cause no symptoms.

The number of times worms are found in the extirpated appendix varies; some observers have not found them and others report as often as 48 per cent. Aschoff, in a study of 600 appendices, has found the oxyuris but twice, while Hoepfl reports a percentage of 21; Raillet, 48 per cent.; Cecil and Bulkley, 13 per cent.; Rheindorf, 47 per cent.; Sagredo, 22 per cent.; Innes and Campbell, 17 per cent. The variance in the figures is explained by Riff as being due to the fact that some authors have dealt entirely with children's appendices, where the oxyuris is more frequently found, but in part, the variance is due to the technic of examination.

Riff, from his personal studies, believes that the oxyuris plays a very important role in the production of appendicitis, as high as 80 per cent. of the cases being infected with the parasite. He thinks that in the near or distant future medical men will study more closely the stools of their patients and will, by discovering signs of the oxyuris, be able by medical measures to remove the worm and that appendicitis will cease to be as common as it is at present.

A rather interesting observation is that of Crichlow<sup>45</sup> who reports a case of appendicitis in the Solomon Islands. The patient had been "Christianized" and "Europeanized," after which she had left off eating native foodstuffs and began to eat European food. Crichlow believes that the change in her nourishment must account for her attack, since appendicitis is unknown among natives living solely upon native foodstuffs.

Malcolm<sup>46</sup> calls attention to the occurrence of appendicitis in the absence of any protective stiffening of the abdominal wall. The absence of rigidity in his case was due to a retrocecal appendix and to former attacks which by producing adhesions had prevented a spreading peritonitis.

CHRONIC PSEUDO-APPENDICITIS. Under this heading, Grégoire<sup>47</sup> speaks of those cases of so-called appendicitis who have a return of all their symptoms after the appendix has been removed. If one examines such a patient, there will be a slight enlargement of the right iliac fossa, with increased tenderness on palpation, which is augmented by pressing hard with the finger tips. This provokes a contraction of the cecum and

<sup>45</sup> Journal of Tropical Medicine and Hygiene, January 15, 1920, p. 22.

<sup>46</sup> British Medical Journal, March 27, 1920, p. 432.

<sup>47</sup> Paris médical, May 10, 1919, p. 379.



colon, and one becomes aware of an elastic swelling in the iliac fossa. Percussion gives a tympanitic note. The remainder of the abdomen is negative. One should suspect a cecocolic dilatation, and an x-ray should be made.

Normally, twenty hours after a barium meal the cecum should contain only traces of the salt, but when there is dilatation, the barium is delayed in its transit and may be seen as late as sixty-four hours. Barium enemata are very useful. The ascending colon is seen very much dilated, while the transverse and descending colon are seen to be of their normal size. This condition has received the name "cecum mobile," "ptosed cecum" and "typhylatony." This dilatation is caused in the great majority of the cases by pericolic bands which are either inflammatory (acquired) or congenital, and the bands causing obstruction to peristalsis account for the discomfort of which so many of the patients complain. Treatment is, of course, operative.

An article devoted entirely to membranous pericolitis and its relation to chronic appendicitis is published by the same author.<sup>48</sup>

It is but an elaboration of the article reviewed above with illustrations and case reports.

### THE INTESTINES.

**Diverticulitis.** Early in this year a general discussion of diverticulitis was held by the section of proctology of the Royal Society of Medicine. Telling,<sup>49</sup> who introduced the subject, said that today the situation was the same as in 1917, when he wrote, "Diverticulitis is a condition which has now passed out of the realm of doubt and uncertainty into that of proved and accepted fact. It has an important place in medical literature, and in the experience of every operating surgeon of large practice. This last statement is not as yet true of all clinicians, some of whom are still apparently unaware of the condition, and not a few of its frequency and clinical importance. Not until a morbid condition is described in all the ordinary student's text-books of medicine and surgery can it be said to have obtained complete recognition, and this is not yet the case with diverticulitis." By diverticulitis is meant any inflammatory change in any diverticulum or series of diverticula. In practice, however, usage has restricted the term to the inflammatory changes and secondary pathologic processes generally occurring in, or in connection with, a certain type of diverticulum. This type is the secondary acquired, multiple, false diverticula of the *large* bowel, nearly always found in the sigmoid flexure. Usually occurring in small or great numbers in the lower part of this structure, they may, nevertheless, be found elsewhere, as in the descending colon, the other flexures, the cecum, the rectum or throughout the entire large bowel. It is of the typical sigmoid flexure lesion that Telling speaks in his paper.

Historically, diverticulitis is new. In 1898, Graser cited examples associated with fibrous hyperplasia, causing stenosing tumor formation *peridiverticulitis*. Similar cases were then described in America, and

<sup>48</sup> Archives des mal. de l'app. digestif, 1919, x, 129.

<sup>49</sup> Lancet, January 10, 1920.



Patel, in France, in 1911, drew particular attention to the more acute inflammatory lesions, sigmoiditis and peritonitis. Following the paper by Moynihan, of a case of the Graser tumor type, Telling began a study of the condition, and in 1908 published an article in which, for the first time, an attempt was made to analyze and classify the cases. The reasons why the condition so long escaped medical attention, are three: (1) Failure of demonstration of morbid anatomy to devote particular attention to the sigmoid flexure. (2) The diverticula conceal themselves. (3) The secondary pathologic processes are apt to be so extensive and disproportionate to the diverticula that the true nature of the case is hidden.

The diverticula are adepts at self concealment; they are small, varying from minuteness up to the size of the last joint of the little finger, more commonly one-third to one-fifth of this size. Their apertures are often minute, from one-sixteenth to one-third of an inch in diameter, occurring in two rows, mostly opposite the appendices epiploicæ and being often concealed by the mucous membrane. From the outside the diverticula are rarely seen because, (1) they mainly enter the appendices epiploicæ, (2) the gut in which they occur is very frequently fat laden, necessitating careful dissection to discover them at all. Once the diverticula are "in being" the whole series of possible consequences depends upon three facts, (1) being formed by pressure from within they tend to enlarge, (2) they tend to harbor fecal or other harmful contents, (3) they tend to undergo various secondary pathologic processes.

In their enlargement they become flask-shaped, with a bottle neck, and this bottle neck may greatly elongate, its lumen remaining very narrow. This elongation is brought about by peridiverticular hyperplasia. The narrow mouths tend to promote retention of soft fecal contents or actual concretion. These contents form a bacterial nidus, a reservoir of toxins and a source of mechanical irritation, and secondary processes result. These are: (1) Ulceration of the mucosa of the diverticula. (2) Perforation. (3) Adhesions when combined with (2) leading to fistulous communication. (4) Peridiverticular fibrous hyperplasia leading to tumor formation and stenosis of the bowel.

The *clinical manifestations* must of necessity be protean. In the first place, mucosal ulceration will weaken the wall of the sac, perforation is facilitated and a concretion being driven through, general peritonitis results. The mucosal ulceration furthermore sets up inflammation on the outer surface of the diverticulum, leading to adhesions which may produce no important results, but which may cause vesical or pelvic syndromes. Fistulous communication with the bladder is the commonest instance. The culminating interest is reached in the peridiverticular hyperplasia, which may exist with mucosal ulcerations of the diverticulum but not infrequently occurs without it and this is the condition which first led to systematic investigation of the subject. Peridiverticular hyperplasia is due to a chronic leakage of toxins or bacteria or both, through the walls of the sac, producing a hyperplastic fibrous tissue-formation similar to that found in hyperplastic tuberculosis of the cecum or scirrhus cancer. A tumor is produced, and because of its fibrous

nature it contracts, stenosis results and chronic intestinal obstruction results. It mimics cancer, and this accounts, Telling believes, for many of the cases of "cured" cancer in this region. It has a relationship to true cancer for a simple peridiverticular stenosis may develop a secondary cancer, as is the case (or as is supposed to be the case) of a chronic gastric ulcer.

The secondary processes can be divided into two groups: A. Mechanical; B. Inflammatory.

#### A. *Mechanical.*

1. Formation of fecal concretions in the diverticula.
2. Lesion of the diverticulum.
3. Lodgement of foreign bodies within the diverticular sac.
4. Perforation.

#### B. *Inflammatory.*

1. Diverticulitis. (a) Gangrenous. (b) Acute. (c) Subacute. (d) Chronic. (e) Latent.
2. Passage of organisms without perforation.
3. Peridiverticulitis, chronic proliferative inflammation with tendency to stenosis of the bowel.
4. Perforation of the diverticula giving rise to (a) general peritonitis, (b) local abscess, (c) fistula, especially into the bladder, (d) suppuration in a hernial sac.
5. Formation of adhesions especially in (a) the small intestine; (b) bladder; (c) female genitalia.
6. Chronic peritonitis—local.
7. Chronic mesenteritis of the sigmoid loop.
8. Metastatic suppuration.
9. Secondary carcinoma.

As far as the clinical symptoms are concerned, they will be those of (1) Inflammatory trouble or tumor in the left lower abdominal quadrant, (2) general peritonitis, (3) intestinal obstruction, (4) Mimicry of carcinoma. The frequency of tumor or abscess formation in connection with any or all of these occurs in 30 per cent. and any case above the age of thirty presenting these symptoms calls for a mental reservation as to the possibility of a diverticular origin; cases occur mostly at, or after middle life, in males more frequently than females, usually with a history of constipation and very rarely blood in the stools.

The *diagnosis* is difficult, and all special aids to diagnosis must be requisitioned. These include (1) the sigmoidoscope, (2) the cystoscope, (3) x-rays. Carcinoma must be differentiated and the following summary of the chief points may be of use:

1. The absence of the shadows of malignancy from the general picture.
2. Tendency to obesity and maintenance of good nutrition generally.
3. Long history of attacks of abdominal pain in the left lower quadrant.
4. History of tumor formation with subsequent disappearance.
5. Absence of blood (visible to the naked eye) in stools over a prolonged period.
6. Presence of a vesical fistula, in which malignancy can be excluded by cystoscopy.

7. Negative sigmoidoscopy as regards malignant disease.
8. X-ray demonstration of diverticula.
9. Pyrexial attacks.
10. Examination of blood, the presence of neutrophilic leukocytosis, and the absence of the specific nuclear changes characteristic of cancer.

Other conditions to be considered in arriving at a differential diagnosis are (a) sigmoiditis; (b) hyperplastic tuberculosis; (c) actinomycosis; (d) syphilis; (e) pelvic conditions generally. Treatment is radically surgical.

Sir John Bland-Sutton, in the discussion which followed the reading of Telling's paper (a full report of the symposium is to be found in the *British Medical Journal*, January 17 and 24, 1920), said his interest was aroused when trying to explain the phenomenon known as "spontaneous disappearance of abdominal tumors." Certain localized swellings in the belly disappear under expectant treatment and the phrase quoted above also disappeared from medical phraseology when it was learned that acute and chronic diverticulitis mimicked many important lesions, especially acute or chronic appendicitis, cholecystitis, gastric tumors, subdiaphragmatic abscess, perigastric abscess, splenic abscess, tubal infections, ovarian abscess, cancer of the uterus and infected uterine fibroids. He recommends medical prevention, saying it should be the duty of the family medical attendant to encourage men and women after middle life to have efficient sets of teeth, and warn them against gobbling indigestible food or bolting hot and unpalatable morsels.

Spriggs said that radiography will fail to show diverticula if they did not stand out in profile, but were behind or in front of the main bismuth mass. Also the bismuth might fail to enter the diverticulum if it were filled with fecal material. In a series of 1000 cases only 6 were diagnosed by the x-ray.

Professor Marison strongly objected to the term "diverticulitis," claiming it was a misnomer and liable to cause confusion between the condition under discussion and the congenital sac called "Meckel's diverticulum." He recommended the term "sacculitis" which Bland-Sutton had already denounced as "ugly and cacophonous."

Normal sacculations must be distinguished from the acquired, the latter being multiple, had no special blood supply, were found in elderly people and were common to all hollow viscera. The only resemblance between the two was the liability of complications, such as gangrene, perforation, etc.

The *etiology* was discussed by Miles, who discredits the idea of congenital origin, as did Morison because of the fact that diverticula often existed in considerable numbers. Increased intracolonic pressure causing hernial extension of the mucosa through the muscular coats at the weak points of bloodvessel perforation, was a much more likely cause. He doubted the part played by flatulent distention as a contributing factor. Intracolonic pressure may be increased by (1) forcible contraction of the sphincter in order to overcome the desire to evacuate the bowels at an inconvenient moment, as when hurrying to catch the morning train. (2) Straining at stool in order to force a formed motion through a narrowed anal orifice. (3) Habitual use of very large enemata.



Norbury laid stress on enterospasm as a factor. This was accompanied by hypertrophy of the bowel wall and increase of pressure. The large amount of fat that accumulated round the bowel in these cases was possibly the result of venous congestion produced by enterospasm.

**Chronic Intestinal Stasis in Children.** "Chronic intestinal stasis is liable to be regarded as a condition affecting maturity because it is generally after this stage of life has been reached that patients present themselves for treatment, but only a few, if carefully questioned, fail to give a history which leads to the suspicion that their condition started in childhood or early infancy."<sup>50</sup> The above paragraph is my excuse for trespassing on the preserves of another writer for *PROGRESSIVE MEDICINE*. If, as Taunton says, we can recognize the condition in children, and if the condition can in some cases be prevented, in some cured, and in others improved, we shall see fewer of these chronic invalids in adult life. At an early age a large number of cases can be cured without operation. Taunton classifies chronic intestinal stasis as follows.

I. *Congenital.* At some point in the bowel there is a shortness of mesentery relative to the rest, producing a kink most marked in the upright position, that portion of bowel being held up by this short mesentery at a higher level than the rest. This kink forms a control to the easy passage of intestinal contents. Most frequently the congenital cases are caused by the mesentery of the appendix taking its origin higher up, and preventing the full descent of the cecum from its position under the liver. They may be due also to the mesentery of the appendix arising from an attachment more toward the middle line and controlling the last few inches of the ileum.

II. *Acquired.* The kink in these cases producing the control is caused by the formation of bands or membranes, often developed in conjunction with the congenital variety.

III. *Neuropathic.* This form is characterized by great lengthening of the mesentery and dropping of the bowel: the transverse colon often lying in the pelvis, the length of the transverse and pelvic colon is increased. Its cause is probably some faulty development of the nerve supply probably at the point where the splanchnic gives place to the systemic.

In a large proportion of cases of chronic intestinal stasis in children it will be observed that their carriage of body is that which is so adequately described by Lane as the symmetrical posture of rest. It is the attitude assumed during temporary tiredness of the trunk muscles, and during permanent weakness or loss of tone. The lumbar curve is diminished and the dorsal increased. The lower ribs are less prominent and their downward obliquity is so pronounced that laterally the rib margins approach the iliac crests and the xypho sternal notch is narrow and long. The upper half of the abdomen is constricted and the lower protuberant. During rest, breathing is diaphragmatic, and only during exertion does costal breathing come into action to a small extent. The assumption

<sup>50</sup> Daunton: *British Medical Journal*, December 20, 1920.

of this attitude lays the foundation for the conditions causing stasis and unless means are taken to correct the faulty posture its course is progressive. In assuming this posture, the intestines tend to lie at the lowest possible point, pushed down by the descent of the diaphragm to the extent allowed by the stretching of the lower abdominal wall, and returning on relaxation of the diaphragm by the elasticity of that wall. They lack the greater range of movement imparted upward by the suction force produced by costal inspiration and downward by the impulse of the muscles attached to the ribs during expiration. The effect of this is that the bowel tends to be continually forced down and to drag on its mesentery; where the lines of force are produced, fibrous bands are formed and in those places where two peritoneal bands are deprived of movement between their apposed surfaces, namely, the under surface of the mesentery of the terminal loop of the ileum with the parietal peritoneum covering the iliacus and psoas muscle on the right side and the under surface of the mesentery of the sigmoid and corresponding peritoneum of the left side, there the peritoneal endothelium will atrophy from disuse of its function, and will be replaced by fibrous tissue which will bridge the potential space between the two layers of peritoneum and account for the two conditions—stellate glistening patches and trapped peritoneal spaces.

The difference between nasal and oral breathing is simply one of resistance. In a nose breather the chest expands during inspiration by the action of the muscles attached to the chest wall, and the abdomen retracts in its lower part. In a mouth breather the chest does not expand, or but very slightly, but assumes the position of full expiration. The abdomen protrudes during inspiration as the diaphragm contracts and in expiration retracts. The alteration in the shape of the abdominal cavity and the change in position of its freely movable contents are reversed in the two forms of breathing, due to the resistance to the passage of air through the nasal passage being cut off in mouth breathing. Mouth breathing in children seems to have a considerable influence in the formation of the bands and membranes of stasis, and nasal obstruction from hypertrophied tonsils is the common cause. Lowering of muscular tone is a frequent cause of mouth breathing because not only in this state does the child hold himself badly, but he finds there is less effort involved if he breathes through the mouth.

Taunton goes on to say that the symptoms of chronic intestinal stasis are many, which is not surprising when we consider that the symptoms are due to auto-intoxication, the development of microorganisms ordinarily not found. "There is one type of individual markedly tolerant to the action of intestinal poisons and in whom a great degree of auto-intoxication may exist without any of the cardinal symptoms being apparent. These people have red, or fair hair, and in them the loss of fat, the skin changes, and the mental disturbances are slight, but the circulatory are in evidence. Persons with dark hair go to the other extreme and exhibit little resistance to this toxemia."

After describing at length the symptomatology, which differs but little from the well known descriptions of Lane, Taunton proceeds to the



diagnosis. Inspection of the abdomen in typical cases shows that it is narrow, flat above, and protuberant in its lower part. One or two permanent transverse wrinkles of the skin above the umbilicus are often to be seen and one, rarely two, half-moon shaped wrinkles, with the concavity looking upward, below the umbilicus. These wrinkles are due to a tonic contraction of the muscles of the anterior abdominal wall, in turn due to some constant tenderness of the intestine (congested loop in stasis). The right side of the abdomen is more resistant than the left, and there is some muscular rigidity in the right iliac fossa guarding the tender appendix and terminal loop of the ilium. X-ray examination determines the true state of affairs.

Treatment should be along the line hinted at in the discussion of the cause. Rest, physical exercises, tonics, change of air, removal of the nasal obstruction, care of the bowels, and finally operation, all have their place in therapy.

**Radiology in Chronic Intestinal Stasis.** In man the viscera are kept in their place normally by the muscles of the anterior abdominal wall, which retains in health their tone when the individual is upright. With Taunton, Jordan<sup>51</sup> believes the adverse cycle which leads to stasis starts in early infancy, artificial feeding leads to overfilling of the stomach, and when it is overloaded it weighs down the transverse colon, whose contents solidify and stagnate. The tension thus exerted on the mesentery, interferes with peristalsis, and in attempting to void the solid feces, straining occurs and leads to elongation of the pelvic colon. Thus stasis commences, and pursues its evil course unless corrected. Great elongation of the pelvic colon is found in subjects of stasis which can be demonstrated by a barium enema. Usually, in health, with the individual lying flat, and the douche bag raised a foot or two, the fluid runs up readily, filling the entire large bowel within two or three minutes. When stasis exists some fluid enters the small intestine due to incompetence of the ileocecal valve.

If the abdominal muscles are exhausted, they relax, and the viscera fall. In strong, healthy, young subjects this occurs as the result of sporting competitions, and Jordan has found prolapsed colons in the members of a football team. In these cases, prolonged exertion was required to fatigue the abdominal muscles, but in stasis these muscles are depreciated by the bacterial toxins and in this state the muscles give out after a short and moderate exertion. When the abdominal muscles fail, the mesenteries act as ligaments and support the intestines, but they are not suitable to act in this capacity and one of two results follows: Either (1) the mesentery refuses the new function and slips down from its attachment or, (2) it makes an effort to adopt itself in its new role and becomes thickened where the strain is greatest, with the result that some parts of the bowel are held up at their proper level. In the first event we see the phenomena presented in Glenard's description of visceroptosis, where not only do the intestines drop but the other viscera, notably the kidneys. The result of the dropping is to force the heavier

<sup>51</sup> Lancet, April 3, 1920, p. 756.



of the viscera to the lowest level they can reach, in some cases the true pelvis, where, by pressure, they excite symptoms attributable to these organs.

The second result follows in more robust subjects when nature attempts to prevent the fall by the formation of new bands—the kinks and membranes of Lane—which represent the crystallization of lines of force. First, they form a local thickening in the mesentery at the points of greatest strain, and developing, their attachment extends around the circumference of the bowel, until, finally, they form firm bands attached to the parietes by the circumference of the bowel opposite to the mesenteric attachment. The first of these bands is formed in the left iliac region, and the new bands may support the bowel at a single point only, or they may extend to the whole length of the left iliac fossa attaching the bowel firmly to this fossa. The splenic and hepatic flexures are also liable to form attachments to the parietal abdominal wall. Lane's kink, is the ileal kink, which forms at the end of the ileum, either close to the ileocecal entrance or at some point along the last six inches of the small intestine, fixing, in some cases, the appendix, and constituting an anchor which holds the cecum at its proper level. Another band descends from the lower border of the liver in the region of the neck of the gall-bladder, then expands, fan-like, with its lower border attached to the hepatic flexure and the first part of the transverse colon. This band falls in front of the pylorus and is in most cases attached to the pylorus, being anchored by it when the stomach becomes loaded with food. In some cases the band is found to continue below the transverse colon and may terminate in an ileal kink, or may even descend to the pelvis and become attached to the right ovary. Bands and kinks not only produce mechanical obstruction but also cause general spasm, not local, of the bowels from their nature as an irritant focus. Spasm is most pronounced at the ileocecal entrance, leading to general thickening and hypertrophy of the last six inches or so of the small intestine, accompanied in many instances by dilatation.

In slight cases of fall of the cecum it can be raised while the patient is recumbent, but falls when he stands. In severe cases, the cecum falls to the deepest part of the pelvis, where it becomes impacted and cannot be raised in any posture of the patient. In the worst cases the ascending colon follows the cecum into the pelvis and drops in front of it. The terminal ileum is found in these instances to be dilated and tortuous, and exhibits an abnormally powerful peristalsis. There is spasm at the ileocecal entrance sometimes amounting to a tight obstructive spasm. Within an inch of the ileocecal entrance there is an irregularly constricted portion, where the barium is seen to flow back through the coil instead of completing its journey into the cecum. This is due to torsion of the ileum brought about by the backward rotation of the cecum in the pelvis. Ileal torsion causes ileal stasis for, (1) the torsion causes a mechanical narrowing of the lumen of the bowel; and (2) it interferes with the vascular and nervous supply of the coil to such an extent that partial paralysis of the constricted portion of the coil is produced; (3) it induces chronic irritation in the coil and sets up spasm at the ileocecal

entrance. In most cases the proximal portion of the appendix is directed upward and backward from the inner and hind wall of the cecum, and in this position is almost certain to cause a hindrance to the passage of the ileal contents into the cecum.

Colitis, which is "nature's attempt to evacuate the stagnant fecal matter by secreting mucus in the bowel" is the evitable result of stasis. If colitis is unrelieved, it may lead to new growth, which may arise in the cecum, hepatic or splenic flexures, or in the iliac or pelvic colon. If the iliac colon is fixed in the left iliac fossa (Lane's last kink) and if the bowel wall is infiltrated with fat, the mucous membrane is forced through the interstices of the bowel wall and diverticulitis results (q. v.).

The congenital undescended cecum is another cause of ileal stasis. The condition cannot be recognized clinically and is often overlooked by radiologists. In the early weeks of fetal life, the cecum lies in the epigastrium in front of the lower part of the duodenum, and as the bowel grows in length it moves to the right until it reaches the liver; thence it follows the lower border of the liver down to the right flank, where it lies in front of the right kidney, separated from it by some coils of the small intestine. Before reaching its final position in the right iliac fossa, the coils of small intestine fall allowing the cecum to come in contact with the posterior abdominal wall, and here it acquires adhesions which keep it in position. Occasionally it happens that the small intestine falls away from behind the cecum prematurely, allowing the cecum to make contact with the posterior abdominal wall at a level higher than the normal, and the cecum becomes at once adherent to its abnormal position. With the continued growth in length of the large intestine the ascending colon droops below the cecum which becomes inverted. The terminal coil of the ileum is the one portion which cannot escape when the rest of the small bowel falls from behind the cecum, for it is attached to the cecum at the abnormally high ileocecal entrance. This coil is imprisoned and caught in the bands which bind the cecum to the posterior parietes.

The causes of ileal stasis are, then: (1) Lane's ileal kink; (2) the controlling appendix; (3) the dropped cecum with ileal torsion; (4) the catarrhal cecum (colitis) with spasm at the ileocecal entrance; (5) the congenital inverted cecum with the terminal ileum retroperitoneal. The results are the same in all cases, namely: (1) overloading of the lower coils of the ileum and dropping of these coils into the pelvis; (2) continued traction on the mesentery of the small intestine, causing it to fall little by little, from its line of attachment along the posterior parietal wall until the dropping includes all parts of the small intestine and a kink is produced at the duodenojejunal junction; (3) this kink leads to distention of the duodenum.

In addition to these mechanical results of ileal stasis, there are other consequences of the gravest importance, chief among them being microbic invasion. This in turn produces its effects in two ways: (1) a general toxemia which renders every tissue of the body unhealthy and vulnerable to the attacks of invading microorganisms; (2) locally, in the digestive tract, where the microbes invade the duodenum and even the stomach.

The invasion by microorganisms of the distended duodenum leads to congestion of the mucous membrane, and then to ulceration. Cholecystitis and pancreatitis may follow. The invasion of the microbes determines the onset of gastric ulcer at the pylorus or in some other part of the stomach. Jordan then deals with the widespread evil results of stasis, subscribing *in toto* to the teachings of Lane which are generally known to readers of PROGRESSIVE MEDICINE and require no repetition here.

**Treatment of Mucous Colitis.** According to Bastedo,<sup>52</sup> the three outstanding manifestations of mucous colitis are abdominal pain, intestinal putrefactive toxemia, and neurotic manifestations. Usually, the patients seek a physician not because of the colitis, but rather for persistent constipation. Abdominal pain or distress, lack of physical energy, obstinate and recurrent headache, failure of physical or intellectual vigor, mental depression or complete nervous breakdown. Patients commonly do not mention the appearance of mucus unless specifically questioned about this point. Since there is no distinguishing factor other than the mucus, the diagnosis rests on, (1) the observation by the patient of the passage of mucus, either as strings accompanying the feces or as a complete mucus stool; (2) characteristic mucus in a stool submitted; (3) characteristic mucus after a test dose of castor oil or a test colon irrigation; (4) the observation through a sigmoidoscope of a dry mucous membrane in the upper rectum to which are clinging the heavy tenacious sheets of mucus.

A word about the *mucus*. This is tenacious and appears mostly as yellow brown or sometimes black jelly-like masses, or plaques, strings, ropes or scab-like membranes. The strings may be many inches in length, and on being teased out in water prove to be casts of the bowel or broad ribbons. Since the mucus adheres with persistent tenacity to the mucous membrane, it is not uncommon to find blood spots on the expelled mucus, as if it had been torn away like a scab. It contains only a few leukocytes and is without fibrin. Bastedo mentions an odor of dead fish coming from the mucus. In addition to the mucus, quantities of blackish or brownish, gritty, irritating intestinal sand are found. Blood is not commonly present.

**Pain.** At some stage of the disease there is discomfort if not actual pain, ranging in intensity from a little soreness to most distressing colic. Its location may be variable or constant; at times the whole colon or a part of it may be tender. The colic is the result of an attempt to expel long retained and clinging mucus and persistence of the attacks indicates that not all the mucus has been liberated. The mucus, acting as an irritant, causes spasmodic contraction of a portion of the colon, and the pain is due to tension in the distended portion above this. Bowel pain comes from distention, not from contraction (Hurst) and the pain ceases after the reestablishment of the peristaltic reflex with dilatation below and contraction above.

<sup>52</sup> Journal of the American Medical Association, 1920, lxxiv, 240.



*Constipation.* Despite the passage of several stools a day, constipation exists, for the cecal cesspool seems never to be emptied. Constipation is not necessarily a condition of infrequent defecation but is one of insufficient or retarded defecation (Hurst).

*Intestinal Putrefactive Toxemia.* "Without doubt the neurotic manifestations and the condition of mental and physical fatigability may in many instances be traced directly to a chronic toxemia caused by the absorption of harmful chemical substances formed in the bowel. And it is probable not only that the constipated bowel of mucous colitis favors bacterial proteolysis, but also that the damaged mucous membrane promotes the absorption of deleterious material. The subject of intestinal toxemia is too large to be dealt with here; it is important to remember, however, that quite often the treatment of mucous colitis involves extensive consideration of the associated toxemia. There may be mucous colitis without putrefaction of the intestinal contents, or there may be putrefaction of the contents without colitis, but the two conditions are often associated." It is regrettable to the reviewer that Bastedo found the subject of toxemia of such large proportions that it could not be dealt with in this paper, for many of us would welcome any suggestions which would assist us in really understanding the subject and diagnosing it should it exist.

Many of the patients have a variety of nervous symptoms ranging from a simple impressionability and hypersensitiveness in insignificant matters to severe nervous breakdown. The colitis is certainly made worse by worry, and may indeed be induced by it. I recall a patient, whose first attack of nervous colitis dated from a harrowing experience at the time of the Titanic disaster. Physical, mental and emotional fatigue certainly play a prominent role in the production and continuance of the disease and hence Bastedo's rule, "Never get tired, physically, mentally or emotionally."

*Treatment.* In determining the method of treatment two facts stand out prominently: (1) retained mucus is harmful mucus, (2) the cure requires a long course of treatment.

I. Treatment in cases without colic or after the attacks of colic. This is designed (a) to prevent accumulations of mucus; (b) to overcome constipation and intestinal toxemia, and (c) to improve the nervous and general health.

(a) To overcome accumulation of mucus, one of the best measures is a weekly purge and colonic irrigations every day or two for a week. Twelve to 24 quarts should be used (hot tap water or sodium bicarbonate, a dram to the pint), the patient lying on the left side for the first gallon of water, and then on the back for the rest of the irrigation. Irrigation is a failure if no water is retained to be evacuated after the irrigation has been finished, or if the water returns clear throughout. When mucus is readily discharged from the bowel, the patient is safe; danger threatens when the mucus stays in and is not readily loosened and expelled.

(b) The treatment of the constipation and intestinal toxemia is that of any form of constipation. Too frequent use of irrigations and enemata should be forbidden; a diet of bran, fruits and coarse vegetables is useful

but in the beginning they may do more harm than a mild tonic laxative. Exercise does not help; if there is ptosis support is needed; water should be drunk freely. The best laxative is usually a softening and bulk-producing one, as liquid petrolatum, cascara agar, phenolphthalein agar, milk of magnesia or salts. The compound licorice powder will be found of benefit. A measure of occasional value is the retention in the rectum over night of from 4 to 16 ounces of olive or cottonseed oil.

(c) Improvement in the nervous and general health. The diet may have to be modified according to the condition of the stomach and upper bowel, and to overlook these is to fail of cure. In general, the diet should be lactofarinaceous, with a transition later to a coarser type with sufficient vegetable and fruit. There should be restriction in the amount of readily putrefactive proteins as found in animal flesh, eggs, beans, peas and lentils, these being replaced by milk. Bastedo believes chicken and egg protein are most prone to produce putrefaction. Any definite associated surgical condition should be overcome. Occupation, recreation and rest should be properly apportioned. Auto-coddling is to be avoided, but rest is necessary as are also early retiring, avoidance of any unnecessary responsibility, serious reading, and physical, mental or emotional fatigue. Tobacco, alcohol and coffee are best tabooed.

II. *Treatment of Attacks of Colic.* This resolves itself into measures (1) to relieve pain and neurotic symptoms and (2) to promote evacuation of mucus. (1) Pain and neurotic symptoms are best combated by rest in bed, a large dose of bromide (2 to 4 gm.), atropin sulphate (0.001), and codein phosphate (0.03). Hot applications in any form are useful. Of all the drugs, atropin is the best for relieving the colic.

2. To promote the evacuation of mucus, castor oil, and colon irrigations are useful. Often the combination of castor oil by mouth, codein and atropine hypodermically, and colonic lavage will be followed by relief and sleep, but if the attack is very severe and if the irrigation is unsuccessful, it is a good plan to put the patient in a knee-chest position and to inject slowly into the colon from one-half to one pint of warm olive oil or cottonseed oil, to be retained over night or as long as possible, a towel being placed over the anus and a rubber sheet on the bed as a protection in case of leakage.

**Tuberculous Colitis.** The text of Brown and Sampson's<sup>53</sup> paper is the early diagnosis of ulcerative tuberculous colitis, and to recognize the condition before symptoms now considered characteristic of the disease, make their appearance—chronic, persistent diarrhea and abdominal pain, tenderness and rigidity. To the authors' minds, such symptoms often occur so late in the course of the disease that a speedy termination of the case can be confidently expected. When a patient begins to do poorly without any increase of pulmonary symptoms or signs, or with even a lessening of pulmonary symptoms and signs, then intestinal complications should be borne in mind. Furthermore, if, under these circumstances, there is extreme nervousness, constipation, slight dyspepsia, a feeling of fullness or discomfort in the abdomen after eating, accompanied

<sup>53</sup> Journal of the American Medical Association, 1919, lxxiii, 77.



by gas, or failure to gain weight under favorable conditions, the probability of intestinal complication is strengthened. These symptoms may be accompanied at times by slight or brief attacks of diarrhea easily controlled by simple remedies and a slight irregular rise of temperature may be noted. With progression of the disease, symptoms increase. In some instances the patient complains of not feeling well, digestion is neither good nor bad, and he may have an irregular temperature, often normal, but reaching  $99.6^{\circ}$  in the afternoon. There may be on palpation, a slight thickening of the colon. The point the authors emphasize is that at this time the symptoms of intestinal tuberculosis may be as slight and as indefinite as those of early tuberculosis.

Severe pain is not an early symptom, but only discomfort is complained of. A little later, pain just below the epigastrium occurs often late in the morning or afternoon, at first transient later more often persistent, crampy and colicky in nature, aggravated by food, relieved by fasting and recurring from day to day. At the beginning, the stools may be mushy and occur once or twice at night, but some have only one loose stool a day, accompanied at times by tenesmus and griping. Constipation, which may be present disappears and the patient because his bowels move without drugs, feels that his "bowels are better." Diarrhea, even lasting six to eight weeks in a patient with pulmonary tuberculosis may be due to other causes than intestinal involvement (irritation of swallowed sputum). As the disease advances, the diarrhea becomes more stubborn and persistent. Diarrhea is rarely present until the disease has extended along the large bowel to the transverse colon, and even then constipation may be marked, but if diarrhea is persistent, it is probable that the transverse colon is involved, though this part of the gut may be affected without persistently loose bowels. Constipation and diarrhea may alternate to the end. The odor of the stools is usually fetid and penetrating, even suggesting to the experienced physician the presence of tuberculous enteritis. Hemorrhage is rare, and is of slight diagnostic value. Flatulence is common, and "gas pains" are frequently described. Some patients have mental depression and unaccountable nervousness. Acute intestinal tuberculosis has been described, but Brown and Sampson have seen no such cases, and believe their acute cases have been due to a tuberculous appendix.

Abdominal examination may show some localized thickening, but this frequently occurs later in the disease and is accompanied by localized tenderness. The latter more often occurs when the ileocecal region is involved, which is the site of the most frequent lesions. Archibald believes that alternating constipation and diarrhea point to lesion of both the small and the large bowel.

*Laboratory Diagnosis.* Many laboratory tests have been devised but none is pathognomonic.

1. *Tubercle bacilli* occur in from 90 to 98 per cent. of all patients with tubercle bacilli in the sputum, irrespective of the intestinal condition.

2. *Pus and blood* in the stools point to ulceration but both may be lacking and ulcers may still be present. Macroscopic blood is rare, and occult blood should be tested for on a meat-free diet.



3. *Blood.* The blood may in rare instances give a picture suggesting pernicious anemia, but the usual characteristic finding is a leukocytosis with a normal relative count.

4. *Tuberculin* may cause some increase of pain but aids little in diagnosis.

5. *Urine.* There may be a marked indican reaction.

*Roentgenologic Examination.* The day before the examination the patient is requested to abstain from taking a laxative. At an appointed hour the next morning he is given a barium suspension on an empty stomach (1 tablespoonful of cocoa, 1 tablespoonful of sugar, 1 tablespoonful of flour, 4 ounces of barium and milk to make 16 ounces). Six hours after taking the meal, the patient is examined fluoroscopically and roentgenographically. At this time one should visualize the cecum and probably the ascending colon. An examination every half hour for the next hour or two may be necessary in order to catch the cecum partially or wholly filled. Another examination is made at the end of eighteen hours and again at twenty-four hours. A day or two later, following an ounce of castor oil eighteen hours before, a barium enema is given and the injection observed with the fluoroscope. When the enema has reached the cecum or has passed through the ileocecal valve, it is stopped and a plate is made in the prone position.

*Normal Motility.* Normally the stomach empties itself in from three to six hours. The head of the barium meal reaches the ileocecal valve in from one to three hours. The ileum empties itself in from five to nine hours. The cecum is seen in from two to four hours after the ingestion of the meal, and six hours after the meal has been taken, the head of the colon is seen at the hepatic flexure or the splenic flexure. Complete evacuation of the meal takes place in from thirty-six to forty-eight hours. The cecum remains well or partially filled from the fourth to the thirty-sixth hours.

*Pathologic Hypermotility.* Complete evacuation of the bowel often occurred in Brown and Sampson's cases in from twenty to twenty-four hours; in many cases, usually the more positive, in six hours the head of the barium column could be seen in the sigmoid and rectum while at the same time there was a small retention in the stomach. On close examination, the authors found that the cecum or cecocolon was the seat of this definite hypermotility. Control cases, with and without catharsis failed to show the hypermotility. Another manifestation which is probably more important than the hypermotility was.

*The Filling Defects.* There was observed a spastic appearance of the portion of the bowel involved, usually the cecum or cecocolon. The smooth haustral sacculations were absent and the bowel had a distinctly irregular and ragged appearance. Under the fluoroscope, barium was seen to enter the diseased cecum, but a few minutes later it had passed on to the transverse colon. This phenomenon was not seen in any condition other than tuberculous colitis.

*Barium Enemata.* With the administration of the enema the barium moved slowly until it reached the suspected portion of the bowel. It was necessary to increase the gravity pressure, or to manipulate the

part. The filling in many cases was only temporary, for there was evident spasm or collapse of the bowel, and the barium column moved distally rather rapidly.

The conclusions of Brown and Sampson are:

1. Tuberculous colitis can be diagnosed clinically with a considerable degree of certainty when the disease is far advanced.

2. On the other hand, in the early or latent stages, when remedial measures may prove of avail, the clinical picture may be of little aid in diagnosis.

3. In all stages, certain shadows cast by the barium meal at the end of six, eighteen and twenty-four hours determine definitely the presence of colonic ulcerations, but the absence of such shadows does not absolutely exclude colonic ulcerations.

4. The roentgenologic picture shows hypermotility and spasm, or filling defects.

5. The presence of such a picture in a patient with pulmonary tuberculosis should lead to a definite diagnosis of colonic tuberculosis.

6. Tuberculous colitis occurs far more frequently than hitherto supposed, and must be excluded in all advanced cases and in any early case with any abdominal symptoms, before submitting the case to radical treatment.

7. No examination of a patient with pulmonary tuberculosis can be considered, today, complete without a roentgenologic study of the intestine.

Carman<sup>54</sup> agrees with Brown and Sampson that if tuberculous infection of the intestine is to be benefited, there must be early recognition, and the best means for this is the *x*-ray. He believes, however, that there are no pathognomonic roentgen signs, as the filling defect and absence of the normal barium shadow in the cecocolon are signs of any ulcerative condition. Carman believes that the term hypermotility stressed by Brown and Sampson is a misnomer, as hypermotility refers to the passage of bowel contents, at an increased rate, along the entire alimentary canal. The gap in the barium shadow described by these authors is due to diffuse infiltration of the bowel wall which produces rigidity of the part of the intestine affected.

He regards the opaque enema as being preferable to the ingested meal, since by its means the filling defect and spastic phenomena which are roentgenologic signs of tuberculous colitis can be demonstrated.

**Roentgen Examination of the Abdominal Organs Following Oxygen Inflation of the Peritoneal Cavity.** An excellent review of the literature is given by Stein and Stewart<sup>55</sup> in this, the first American paper on the subject. The patient is prepared in the usual manner for roentgen examination, is put flat on the back and the abdomen inflated with 3 to 4 liters of oxygen. The needle is inserted under aseptic precautions, in a spot 2 to 3 fingers to the left and about one and one-half inches below the umbilicus. Introduction of the gas takes about five minutes for a gallon of gas (3 to 4 liters). When the abdomen is entirely distended

<sup>54</sup> Journal of the American Medical Association, lxxiv, 1371.

<sup>55</sup> Annals of Surgery, 1919, lxx, 95.

the patient usually complains of a sensation of fulness and slight pains in the shoulders (the latter apparently due to pressure against the diaphragm). As far as the fate of the oxygen is concerned, it is usually absorbed without any trouble within twenty-four hours.

Alvarez<sup>56</sup> regards this method as the biggest advance in radiologic technic since the introduction of the bismuth meal by Cannon in 1898. He is convinced of the harmlessness of the procedure from his experiments on animals, but seeking a method applicable to all patients rather than to those in the hospital, he injected CO<sub>2</sub>. This gas is absorbed in twenty-five minutes and the only disadvantage is that one must work extremely fast. It may be used to advantage in the office.

A French contribution by Mallet and Baud appears in *Le Progrès Médical*, December 20, 1919, p. 507. They use but 2 liters of oxygen and state that with even 1 liter the contrast is well marked. Absorption is accomplished in forty-eight hours at the most. They claim that the gas causes no inconvenience and is well tolerated. When the patient stands or is seated a mild pain is complained of in the right shoulder, due to pull on the coronary ligament of the liver. Injection of oxygen can be made even in dyspneics without further embarrassing the respiration. Inflammatory states of the peritoneum are the only contraindication to the employment of peritoneal inflation. Mallet and Baud claim that their injections are controlled by manometric readings and state that when there are adhesions the limit of the amount of gas can be determined in this way, but, unfortunately, they give no figures indicating the safety or danger point.

A personal experience with the method is vividly described by Whitman.<sup>57</sup> The procedure described by Stein and Stewart appealed to him as offering a brilliant opportunity for a demonstration of the effect of posture upon the internal organs. It is believed that posture has a definite effect on the position of the liver, kidneys, colon, etc. "Almost any one will grant that a person standing in a slouchy attitude, with the chest flat, back hollow, and abdomen prominent, is more likely to suffer from floating kidney, or intestinal stasis, for example, than are those who stand erect, aerate their lungs, and give their viscera at least a modicum of outside support. If we might show, however, a roentgenogram of the liver forced well up against the diaphragm, and the spleen and the kidneys back in their respective beds, all brought about by a change in the erect attitude, the demonstration would be as nearly final as one could ask."

Whitman, therefore, determined to make such studies upon himself. Realizing from a communication from Stewart that there were some unpleasant features connected with the method, that it produced a sensation of distention, and occasionally some pain between the shoulders, Whitman nevertheless had an oxygen injection given. The purpose for which the experiment was tried was a failure, that is, there was no apparent change in the position of the organs when he assumed various postures. The interesting part of the article is that describing his

<sup>56</sup> California State Journal of Medicine, 1920, xviii, 42.

<sup>57</sup> Journal of the American Medical Association, 1920, lxxiv, 1021.



sensations during and after the administration of oxygen. The actual injection of the gas was practically painless, but the subsequent mechanical effects were decidedly unpleasant.

After ten minutes liver and splenic dulness was obliterated and a fairly marked feeling of distention was apparent, and in about fifteen minutes, a dull aching pain began between the shoulders and the injection was stopped. At this time the abdomen, from having been almost scaphoid, was no more than flat, there was no appearance of distention, but the abdomen was tympanitic, the lumbar gutters being the last regions to become so. There was no alteration in pulse or respiratory rate, and an x-ray taken in the supine position showed a fairly even distribution of gas, but not as clearly as Whitman had been led to believe. When he attempted to stand up, the feeling was no more than uncomfortable, but during the next ten minutes, while the pictures were being taken, he became conscious of increasing distention and discomfort, and he lay down. Rising now was most uncomfortable, and the feeling of distention increased, and while getting his clothes on and walking to the door, he found himself walking with extreme care and trying to avoid every jar.

On going out of doors on the way home, the discomfort became much greater, the chest was held in mid-expansion, and the breath was held as long as possible and expelled with a grunt, and the movements of the diaphragm were restricted as much as possible. After he had walked one block the discomfort had become a pain, and the apprehension of being bumped or jarred was extreme. "It was literally fear lest a collision or decided jar would cause something to burst." The pain between the shoulders became increasingly severe. Lying down after reaching home gave great relief, the respiratory embarrassment disappeared, but the sense of abdominal distention and oppression in the epigastrium remained. The assumption of the erect posture caused recurrence of the pressure on the diaphragm. Sleep that night was not interfered with.

The next morning, Whitman woke comfortable, but, on moving, the abdominal cramp returned. Dressing was uncomfortable, but it was impossible to bend over to lace the shoes. Walking at a reasonable rate was out of the question, there was return of the apprehension of a jar, and a new pain, this time in the heads of the humeri appeared. For ninety-six hours after the injection, the symptoms remained practically constant. He finally discovered, as time went on, that the most effective remedy for the epigastric oppression was to stand on the head. After a few seconds, the gas would be felt gurgling up into the true pelvis, respiration became easy and the abdominal distress disappeared. Urination was not affected, the bowel movements became loose, and there was some relief after defecation. The gas was absorbed, or at least the symptoms of its presence disappeared, quite suddenly on the fourth day after the injection, although gas bubbles could be felt on the fifth and sixth days. "Short of being totally incapacitated, I have never undergone such an uncomfortable painful and thoroughly disagreeable experience."

Whitman suggests that the injection might not be so disagreeable to a bed patient, but he warns that the method should not be employed unless the patient has been warned of what he might reasonably have to expect and be prepared to spend from three to four days in bed following the injection.

**Limitation of X-ray in the Diagnosis of Gastro-intestinal Diseases.** Roberts.<sup>58</sup> while admitting, of course, the marvelous advance of *x*-ray diagnosis, nevertheless feels that it is necessary to stress the fact that there are certain definite limitations in the method which must be admitted and generally understood. To the limitations as expressed by the great expense incurred, Roberts does not refer, and the rise of the commercial laboratory does not seem to him to solve this problem. He emphasizes the fact that while great progress has been made in the recognition of gross lesions of the abdominal viscera, but comparatively little advance has been made in the study of those visceral changes of a structural nature which are of so much importance and which are so obvious on the postmortem table. Since these changes are not appreciated by the roentgen examination, a negative *x*-ray diagnosis of a gastro-intestinal lesion should never be regarded as final in the exclusion of gastro-intestinal disease.

In the case of the esophagus, the passage of the meal is so rapid through an unobstructed esophagus that an examination of this structure is far from satisfactory. Far more preferable is the direct examination with the esophagoscope. Although the fluoroscope and film are able in a large proportion of the cases to show a gross lesion, nevertheless, there are certain stumbling blocks which must be reckoned with in every examination. For instance, the cardiac end of the stomach fills out poorly, and unless a suspicion is entertained of a lesion in this region it will be overlooked, and he urges the use of the gastroscope. Ulcer and cancer of the posterior wall, unless large and encroaching on the curvatures, fail to give definite filling defects as shown by the plate. Roberts states that early annular growths in the pylorus are compatible with normal roentgenographic appearances. There is, furthermore, a definite group of cases that resemble ulcer, in which, however, the *x*-ray examination is negative. Such cases frequently have a shallow crater-like ulceration, which may be detected but which are not infrequently overlooked. "Positive roentgenographic evidence of ulcerative or indurative lesion of the stomach may contradict all other evidence and negative evidence of a gastric lesion has some weight; but I feel that we should hesitate to accept a negative roentgenographic diagnosis of gastric lesion with a positive history and suggestive laboratory findings unless some other lesion is discovered as a possible cause of the clinical disability." Differentiation between ulcer, cancer and syphilis, while not easy, may nevertheless be made in the advanced case, but it must be remembered that it is not safe to rely on the *x*-ray differentiation alone.

It is now possible to visualize gall-stones in the majority of cases, and frequently the chronic thickened gall-bladder is shown. Not all cases

<sup>58</sup> Journal of the American Medical Association, 1919, lxxiii, 1511.

of stone and thickened bladder can be demonstrated, and a visualized gall-bladder is not necessarily a pathologic gall-bladder. Since in 20 per cent. of the cases, no disease can be demonstrated roentgenographically it seems unwise to make a negative diagnosis of a pathologic condition of the upper abdomen on a negative x-ray examination.

The terminal ileum and cecum offer a fertile field for difficulties, and Roberts has come to regard the roentgenographic diagnosis of conditions in the right iliac fossa with considerable suspicion and he insists that a definite opinion should be expressed only when there is the most unmistakable persistent evidence in support of the clinical picture. The x-ray diagnosis of appendix has recently become most popular. He believes that the failure to fill or to empty when filled, even after several days, is not incompatible with a normal appendix, for he has seen the appendix filled, curved, and somewhat angular, and remain filled for ten days and yet prove normal on removal. Roberts contends that we are not justified in accepting the statement so frequently heard, that the appendix that fails to empty promptly or that is retrocecal, is a dangerous appendix *per se*. As clinicians we are not so much interested in whether the appendix is somewhat abnormal, but whether it is responsible for disability or is a source of danger from acute disease. He is convinced that the after-results are poor in those cases giving no history of definite acute attacks.

"The ideal form of roentgenographic examination of the gastro-intestinal tract resembles the complete necropsy which the pathologist approaches without bias in the effort to discover the exact condition of each part, and later perhaps correlate his findings with the disabilities observed during life. With a reasonable degree of positiveness, conclusions may be reached as to gross lesions of the abdominal organs by roentgenographic examination; but it must not be forgotten that the accuracy of these conclusions depends entirely on the pathologic knowledge, the experience and the scientific honesty of the interpreter, and due allowance must always be made for the limitation of the roentgenographic method of diagnosis."

**Gas Cysts of the Abdomen.**—A brief historical sketch of the subject precedes the description of 2 cases of this strange malady by Tupier and Letulle.<sup>59</sup> The occurrence of multiple cysts in the intestine, omentum or mesentery containing gas has been known only since the beginning of the nineteenth century following the discovery by Mayer of the condition in an otherwise healthy hog, and made its entrance into human pathology in 1825 with Cloquet, Duvernoy, but especially by Bang, a Scandinavian writer, in 1876. The last-named, at the autopsy of a volvulus victim, found the last portion of the ileum covered with transparent vesicles filled with an odorless and colorless gas. Only as late as 1899 was the disease first found *in vivo* during an operation for gastric ulcer. Since that time 66 cases have been reported, including the two now described by Tuffier and Letulle. Owing to the unusual interest aroused by this pathologic curiosity, these two cases are quoted *in extenso*.

<sup>59</sup> Bull. de l'Acad. de Méd., 1919, lxxxii, 5.



Observation 1. A twenty-three-year-old woman, whose medical history comprised a left-sided pleurisy with peritonitis (complete recovery) at the age of sixteen, and typhoid fever at twenty, which left her somewhat depressed and subject to attacks of vomiting, was disturbed in January, 1913, ten months before entering the hospital, by abdominal distention. This distention was intermittent for five months, but after that the abdomen was permanently distended, for four months and the distention was accompanied by attacks of diarrhea, and vomiting. At this time she complained of a swelling in the left side of the abdomen, which of itself disappeared and was unaccompanied by gurgling or evacuation of gas. In August, 1913, on admission to the hospital, the abdomen was found to be large, smooth, with signs of peritoneal effusion, fluctuation and movability, all without any sign of organic disease. The Wassermann reaction was negative. Believing the swelling to be due to tuberculous peritonitis an exploratory puncture was made and a fecal-like fluid recovered. Three weeks later a second puncture was negative. However, during this time there was dulness in the left flank which could be displaced from left to right in the lateral decubitus. Signs of multiple stenoses of the small intestine later developed, and on x-ray examination, a pocket, independent of the stomach, was found in the superior portion of the left lateral abdominal region. The bismuth seemed to collect *below* this air pocket, in the stomach, which was the more remarkable since the stomach descended to the pubis.

On November 19, 1913, an operation was performed because of the fear of obstruction. Upon opening the abdomen, the small intestine disclosed itself, riddled with thousands of little transparent cysts, varying in size from a pin's head to a large pea, confluent, occupying the lower segment of the small intestine but particularly along the free wall, and over an area of more than a meter. On crushing these cysts, they made a report like that of a crushed berry (*baïe de tronène*). Some of these cysts had infiltrated the intestinal wall, and the omentum was covered with similar tumors less numerous and less confluent than in the intestine. When the intestine was compressed to introduce it into the abdominal cavity, it crepitated like emphysema.

Apart from these vesicles, at certain points were two or three encysted effusions of a yellowish liquid, such as is seen in inflammatory states of the peritoneum. Finally, in the lowermost portions of the abdominal cavity, there was a yellowish ascitic fluid, comparable to that seen in ovarian cysts, which coagulated spontaneously. Below these cystic areas of the intestine, the gut was simply dilated, adhesions existing only in the upper part of the abdominal cavity. The pelvic organs and abdominal organs were normal, and animal inoculation for tuberculosis was negative. Nothing was attempted surgically and with rapidly developing signs of obstruction, intestinal and pyloric, the patient died January 12, 1914.

At autopsy, the authors were astonished to find that the gaseous cysts had in great measure disappeared. There was no evidence of ulceration or of cancer in the digestive tract, and the urinary organs were normal.

Briefly the patient had the syndrome of gas cysts of the abdomen with stenosis of the small intestine and pylorus.

Observation 2. The second patient was a man of forty-three, with vague gastric symptoms, of the type seen in hyperchlorhydria. In the middle of 1916, he began to notice abdominal heaviness, and the abdomen began to change its shape. Vomiting became more frequent and an x-ray showed dilatation and ptosis of the stomach without ulcer. Loss of weight was rapid, and the condition resembled that of pyloric stenosis or of a prepyloric ulcer.

In January, 1918, Tuffier saw the man and consented to perform a laparotomy believing the condition to be pyloric stenosis. The small intestine and omentum were covered with vesicles ranging in size from a pin's head to cherry stone, subserous, pedunculated or sessile, and giving to the intestine the feel of inflated cellular tissue. Below the stomach at the first portion of the duodenum an enormous bunch of these cysts formed a tumor mass, and it was this tumor mass which had given rise to the symptoms of stenosis. Profiting by his experience in the first case, Tuffier performed a posterior transmesocolic gastroenterostomy, and the patient made an uneventful and happy recovery.

The evolution of the cysts is interesting. They may persist for a long time, but in the vast majority of the cases they disappear, as exemplified in Observation 1. In one case of Urban, repeated laparotomies were found necessary before the cysts finally disappeared. They are replaced by nodules or by whitish scar-like tissue, and it is not impossible that some of the mother-of-pearl spots seen on the peritoneum and ascribed to plastic peritonitis may have had their origin in these cysts. The differences in the location and number of these cysts, described by various writers, depends upon the different stages of the cyst evolution, and it is possible that those who have reported but one or two cysts in the omentum or mesentery, had seen them in the moment of retrogression, if not ultimate disappearance. It is impossible at the time of operation to remove the cysts, and we can but hope to remove their secondary effects, namely, obstruction. The etiology is unknown, although Tuffier and Letulle quote various theories.

An analysis showed the gas of the cyst to have the following composition:

CO <sub>2</sub>	15.0 per cent.
O	5.6 "
H	73.3 "
N	6.1 "

Two important papers on the pathology of this bizarre condition have been published by Letulle. One, in the *Bulletin de l'Académie de Médecine*, 1919, lxxii, p. 315, deals with the subject very extensively, and with numerous cuts, should be consulted by those interested. It is far too elaborate to permit of reviewing here. The second paper<sup>60</sup> is briefer in scope. He believes that the starting point of these cysts is an obstruction to the flow of the lymph—a chronic obliterative lymphangitis.

<sup>60</sup> Presse médicale, 1919, p. 781.

The content of the cyst is an odorless gas very much like atmospheric air, according to the majority of the writers, but it seems not to have the same composition at all times, for some say it burns with a blue flame, (Artz) and others find it non-inflammable (Nigrisoli, Grvendlhal). All chemists have found oxygen, hydrogen, nitrogen and CO<sub>2</sub> in varying proportions.

Histologic examination has been made by numerous investigators in many countries and all are in accord in their findings. The gas cyst may occupy different places in the intestinal wall—submucosa, subserosa—or in the mesentery or omentum. The shape is generally round, but when there is a conglomerate mass, it may be any shape from reciprocal compression. The structure of the cysts is always the same, it consists of a fibrous tissue base, poor in bloodvessels and in cells, with no smooth muscle fiber. The different coats of the intestine suffer according to the location of the cyst.

In the mesentery, the bloodvessels were contiguous to the cyst seem not to suffer, but the large lymph channels show signs of a notable hyperplasia. It is because of the involvement of the lymph vessels that has led to the belief that the cysts are chronically inflamed lymph vessels distended with gas.

Just what the origin of gas is it is difficult to say! Two theories are offered (a) bacterial, (b) mechanical. (a) The first holds that an organism of the intestinal tube invades the lymph channels and by its gas production causes the cysts. "*Bacterium Colilymphaticum Aërogenes*." This view is held by very recent writers, including Stoyanovitch.<sup>61</sup>

(a) The mechanical theory is that the intestinal gas penetrates into the distended lymphatics, due to minute ulcerations in the mucosa. As Lenormant<sup>62</sup> says, unfortunately there is little or no ulceration in the cases of gas cysts of the abdomen, also the theory is not tenable for the cysts in the mesentery and omentum, also it takes into little consideration the fact that the gas of the cysts is not at all like the intestinal gas.

**Solar Plexus Sign in Gastric Disorder.** The solar plexus is situated in the median line below the umbilicus, at the point where a line joining the ninth ribs crosses the midline, or exactly at the level of the first lumbar vertebra. This point is above the pylorus and the transverse colon. The left and right borders of the stomach are beyond and to the left of the vertebral column, only the pylorus and lesser curvature are at the level of the lumbar vertebrae, but below the solar plexus, at about the level of second or third lumbar vertebrae. When the subject is prone, the stomach ascends a little, and the pylorus can cover the solar plexus, while the transverse colon is always below the plexus.

Patients with the solar plexus sign<sup>63</sup> complain of spontaneous pain in the subumbilical median line. This pain is increased by deep palpation, and, where not, spontaneous palpation will elicit it. The pain does not radiate, and is due to the solar plexus. Pyloric pain and colonic pain in a patient in the erect posture, are below the place where

<sup>61</sup> Thèse de Paris, 1919, and Marthe Lang, *ibid*.

<sup>62</sup> Presse médicale, 1920, p. 104.

<sup>63</sup> Fraikin: Paris médical, 1920, x, 143.



solar pain is complained of, and the pain shifts its position, depending on the position of the patient, which is not the case with the solar plexus pain. If a patient with plexus pain is examined in the recumbent posture, only a slight pain will be felt on palpation, and will have no special characteristic. When he stands, the pain becomes acute, and, when a fluoroscopic examination is made, it will be seen that the pylorus and colon are below the point of pain. Nevertheless, the pain has not shifted its location but has become more exquisite because the solar plexus has become uncovered by the altered position of the pylorus, and hence the palpating hand is more directly touching the plexus.

Another test is to stand behind the patient, and press on the umbilical region with both hands. The walls of the stomach are raised, protecting the plexus and one is able to cause but slight discomfort, often none at all. Pressing on the stomach thus will cause a great deal of pain if the pain is gastric in origin, but none if it is solar. The latter pain is often immediately relieved by lying down, and also by wearing a support. Fraikin believes the pain is caused by pulling on the nerve fibers by ptosis, hence it is seen especially in women, and indicates an abdominal neuropathy. It is a sign of some importance inasmuch as one can by it distinguish between an organic visceral disease and a neuropathy. Treatment is essentially physical—supports, diet, heliotherapy, hydrotherapy, compresses, massage, electrotherapy, thermoluminothrapy.

**Occult Blood.** Seidl<sup>64</sup> has used the duodenal tube to study those cases of ulcer which show no occult blood in the stools, or which, because of hemorrhoids, exhibit blood from an extraneous source which cannot be eliminated as a source of error. He has found that blood can frequently be recovered from the duodenal or gastric juice when none is apparent in the feces. Another advantage which he claims for this method is that it enables one to localize the ulcer either in the stomach or duodenum.

Maselli<sup>65</sup> remarks that to date we have no absolutely specific chemical test for blood in the stools. All the technics in vogue give a positive response with certain other substances besides blood. Microscopic examination of the stools will sometimes reveal substances to which the positive response might be credited. It is not safe to draw conclusions from positive findings unless different technic and repetitions of the tests give concordant responses. A negative response with the benzidin test, when strictly applied and to different parts of the stool, may be regarded as decisive as to the absence of blood from that particular stool.

Gregersen<sup>66</sup> called attention to the fact that the reason why so much criticism had been leveled at the benzidin test on account of its positive reaction in so many cases where no blood could be suspected, was because too concentrated solutions of benzidin where being used. He recommended that 0.025 gm. benzidin and 0.1 gm. peroxid of barium, each, be dissolved in 5 c.c. of 50 per cent. acetic acid. Boas<sup>67</sup> has confirmed the

<sup>64</sup> Arch. f. Verd. Kr., 1920, xxvi, 19.

<sup>65</sup> Abstract, Journal of the American Medical Association, 1919, lxxiii, 71.

<sup>66</sup> Arch. f. Verd. Kr., 1919, xxv, 43.

<sup>67</sup> Berl. klin. Wehnschr., 1919, xxv, 939.

accuracy of Gregersen's observations, namely that when there is no blood, the test is negative, but he raises the question whether, because of the weak dilution of the reagent, there may not be a possibility of overlooking the minimal traces of blood one is anxious to detect. This he believes is the case, but he recognizes that Gregersen's modification of the test is a valuable improvement in technic, with the single exception that the benzidin and barium have to be exactly weighed. To overcome this obstacle, which is a distinct disadvantage, he has had made and supplied by Merck the proper amounts of benzidin and barium peroxid, in tablet form which being added to 10 c.c. of 50 per cent. acetic acid gives the proper strength solution.

**Effect of Heat on Abdomen.** The application of heat to the abdomen is a therapeutic measure of the greatest importance in painful affections of the gastro-intestinal canal; but for a long time no one was quite clear in his own mind as to the physiology of this treatment. Leube, who recommended it in the care of gastric ulcer, stated that, in his experiments, it caused a localized reddening of the gastric mucosa; Penzoldt thought the greatest effect was due to the rest which the treatment demanded (psychic effect), as did Strümpell.

The first thing Ludin<sup>68</sup> attempted to decide was whether heat applied locally could penetrate to the stomach. He used the apparatus of Siemens and Halske, recording variations in temperature on a revolving drum, and found that compresses applied to the abdomen could raise the intragastric temperature 1° C., but the compresses had to be kept on interruptedly for two hours, during which time the intragastric temperature slowly rose. Using an electric cushion, the greatest temperature increase was 0.8° C. after two hours. With a diathermic apparatus, the gastric temperature rose more rapidly, and a maximum of 2.1° C. was reached within an hour.

During the temperature rise, the gastric chemistry was studied, but in numerous experiments no noteworthy change in the composition of the gastric juice could be detected. There were, to be sure, slight individual variations, but these were of little moment. Gastric secretion was also uninfluenced. Gastric motility was studied, and of 14 cases, 12 showed a perceptible increase in motility, so that the emptying time was from one-half to two hours shorter than in the controls. Peristalsis was increased, the waves being deeper and stronger and peristalsis began higher in the stomach than in the controls. This observation is a contradiction of the usually accepted view, that warmth quieted the stomach although it was known that warmth increased intestinal peristalsis. Why this difference could not be explained, heretofore. Experiments on rabbits, with the stomach exposed, showed that heat in various forms, increased peristalsis as it does in man.

Patients with delayed gastric emptying were studied (pylorospasm—pyloric stenosis); 10 patients with organic stenosis showed no increase in gastric emptying despite increasingly strong peristalsis; 9 patients

<sup>68</sup> Ztschr. f. d. Ges. experimentelle Medizin., 1919, viii, 68.

with pylorospasm (gastric ulcer, duodenal ulcer) showed a decided shortening of the emptying time. Ludin believes this observation is of great importance in differentiating pylorospasm and organic stenosis, and he believes the overcoming of pylorospasm by heat with the resulting increased motility explains the good effects of warmth observed in certain gastric conditions. Apart from the pain-diminishing properties of heat, it is a valuable measure therefore in the treatment of gastric ulcer, since accelerated emptying of the stomach will prevent the irritation of stasis, hypersecretion and hyperacidity.

### DISEASES OF THE LIVER.

**Pathologic Metabolism of the Liver.**<sup>69</sup> CARBOHYDRATE METABOLISM. Changes in the carbohydrate metabolism are expressed in various ways: disturbance of glycogen formation or as disturbance of anabolism or catabolism of sugar. An isolated instance of pure insufficiency of glycogen formation is seen when the liver is suddenly overwhelmed by a large sugar intake, and there is an increase in the blood-sugar (alimentary hyperglycemia). The supposition that sugar taken into the stomach passes through the liver in great amounts and does not, by means of the lymphatics, enter the blood stream (anhepatic) has led investigators to use the amounts of sugar found in the urine and in the blood after the administration of glucose, as an index of a disturbance of liver functioning, and especially that having to do with glycogen formation. Newer researches teach us that the appearance or non-appearance of sugar in the urine, despite hyperglycemia, depends largely upon the condition of the kidneys. The increase of sugar in venous or capillary blood is only a relative measure of the amount of sugar unchanged by the liver, since one never knows the amount of sugar in the hepatic vein which is eventually carried to the various depots in the body. Also, the amount of glycogen already in the liver plays an important role. All these points should be borne in mind when one endeavors to deduce from hyperglycemia an index of the amount of disturbance in glycogen building function.

In health, 100 grams of glucose causes a rise in blood-sugar two or three hours later. Studying the blood every ten to fifteen minutes, the curves show a more or less permanent rise, and in only a few cases does blood-sugar show no rise above the control period. There does occur a hypoglycemic phase which is supposed to represent an especial activity of the liver as regards glycogenesis, or a particular avidity of the tissues for sugar. The hyperglycemic phase represents, of course, a physiologic disturbance of glycogen formation due to the large amounts of sugar administered. Having the above in mind, it may be questioned whether one should attach so much importance to alimentary glycemia.

The physiologic insufficiency of the liver after dextrose administration is not encountered or is not so sharply seen if levulose is used. After

<sup>69</sup> Isaac: Berl. klin. Wehnschr., October 6, 1919.



100 grams there is a much lower increase in blood-sugar; in many cases there is no rise above the control period, and a fractional curve shows increasing tendency for the sugar to decrease in amounts. Therefore it may be assumed that levulose is more readily converted by the liver than is glucose. There is reason to believe that about 15 per cent. of the levulose ingested is immediately burned (Neubauer), therefore only about 85 per cent. is changed into glycogen. This belief is strengthened by Benedict's finding of marked increase of  $\text{CO}_2$  after feeding with levulose, and by the observation of Oppenheimer that levulose in the perfused liver is incomparably easier to convert into lactose than is glucose. Again, there is Minkowski's well known teaching that in diabetes levulose is well borne.

In disease, Strauss and Sachs found glycosuria more often after levulose than after dextrose and they believed there was a special disturbance of the liver cell so far as glycogen formation from levulose is concerned. Isaac found, however (work not yet published), that in liver disease the blood-sugar curve is much lower after levulose than after glucose, and after often not much higher than is seen in normal subjects. Although glycogen formation from levulose is perhaps not so easily accomplished as in health, one must not assume that in disease levulose is less easily changed than glucose. One would do better to regard alimentary levulosuria not as a specific functional disturbance of the liver but rather as a change in the permeability of the kidney, as is the case with glucose. In hepatic disease, the hyperglycemia after levulose, is made up for the most part of glucose, and if the blood of such a patient is examined fasting there will be found no more levulose than is seen in health. Isaac believes, therefore, that the elementary function of the liver to convert levulose into dextrose is in no wise interfered with by changes in the parenchyma of that organ.

In diabetes it has been thought, and by some still is believed, that the cause of glycosuria is to be found in an irritation of the liver cell, due either to a primary anomaly of the liver cell, or to excitation of the cell (chromaffin system), or to inhibition (pancreatic). V. Noorden believes that there is a violent stimulation of the no longer bridled diastatic process, and Kolisch believes there is an abnormal formation of sugar from the protoplasm as the result of nervous or toxic stimulation. Normally, in the liver, sugar is being destroyed and being formed, (glucose to lactic acid, lactic acid to glucose) in such a way that neither is lost. The process is reversible—when there is more sugar, lactic acid is formed, when there is a higher concentration of lactic acid, more sugar is formed. In the diabetic liver, Embden and Isaac believe that the balance of metabolism is disturbed in the direction of sugar synthesis without disturbance of the catabolic function. Normally a higher sugar concentration leads to more glycogen formation but in diabetes this does not occur; rather the opposite occurs. After adrenalin injection, there is increase of sugar formation and at the same time an increased conversion of glycogen into sugar, hence we have a sugar richness and glycogen poverty. This is supposed to be due to a physical chemical change in

the cell mechanism (change in cell permeability) whereby the action of diastase on glycogen is facilitated. That it is not due to increase of diastase has been shown by Schirokauer and Wilenko, who found in diabetes no quantitative change in diastase. So, under the influence of the diabetogenous stimulant or excitant, the two reactions are disturbed—the lactic acid  $\rightleftharpoons$  glucose reaction, in the direction of synthesis, and the dextrose  $\rightleftharpoons$  glycogen reaction in the direction of breaking down. In a severe case, both reactions may be determined, in a mild case only the latter is disturbed.

Is there a condition in which the balance between sugar formation and breakdown is disturbed so that there is less sugar formed? In adrenalectomized animals hypoglycemia is seen, and it would be interesting to determine the amount of lactic acid produced, which has not yet been done. In phosphor poisoning there is lessened blood-sugar and increased lactic acid, and it is not unlikely that phosphor influences the sugar metabolism in such a way that the glycogen in the liver cell is rapidly changed into lactic acid.

**Urobilinuria.** Although urobilinuria is a very common symptom its real significance is still the subject of much controversy. Brulé<sup>70</sup> has reviewed the question at length. Many hypotheses have been advanced. Hayem believed that whenever there was any change in the liver the hepatic cell became incapable of changing hemoglobin into bilirubin and then into urobilin, the last named being the pigment of the diseased liver as bilirubin is the pigment of the healthy gland. Moreover, Hayem associated urobilinuria with destruction of the red cells, and in this case there could be urobilinuria without any lesion of the hepatic cell, the latter being unable to effect the customary transformation, merely because of the untoward load thrown upon it. (*Hepatic Theory.*)

In Germany, the *enterohepatic theory* has been preferred to the hepatic theory of Hayem. Bilirubin poured into the intestine through the common duct becomes converted into stercobilin, a pigment identical with urobilin. The stercobilin is normally taken up in part by the portal circulation, but is checked in its further mobilization by the liver. The latter becoming, for one reason or another, insufficient, the urobilin passes into the circulation and thence into the urine. The appearance of urobilin in the urine therefore depends upon two factors, the presence of bile pigments in the intestine and a functional disturbance of the liver.

The *hemic theory* claims that urobilin can be formed directly from hemoglobin liberated by destruction of the red cells. It is known that by means of certain chemical reactions, hemoglobin can be converted into urobilin, *in vitro*, with hematine and hematoporphyrine being formed as intermediaries (Hoppe-Seyler); the same change can be observed spontaneously in sterile blood at 37° (Ajello). Subcutaneous injection of blood (Poncet) and experimental hemolysis (Pellacini, Lesné and Ravant) can provoke urobilinuria. Therefore, if one accepts this theory, it means that urobilinuria has its origin in the blood and is an expression of an abnormal number of red cells.



There is another theory held by some, the *histogenic* or *pigmentary theory*: Urobilin is formed in the tissues by reduction of the bile pigment which may have been deposited there. Urobilinuria, then, according to this hypothesis, is the result of the retention of bilirubin, and is the expression of the defense of the organism against biliary impregnation.

Finally, there is the *renal theory*—Urobilin is formed in the renal parenchyma by reduction of bile pigments retained in the organism. Urobilinuria is an index of cholemia but is not a sign of hepatic insufficiency. It will be seen that this theory is very like the histogenic theory, limiting the activity of the tissues to the kidney, however, while the histogenic theory, be it made clear, claims that all tissues participate in the urobilin-forming function.

Such diverse theories cannot fail to bring confusion, and perhaps doubt, into the minds of those who try to answer the question, does or does not urobilinuria indicate a hepatic lesion? Brulé, in attempting to reply to this interrogation, sets down certain well-established facts that every one believes:

1. There exists, chemically and clinically, a definite relation between bilirubin and urobilin.

2. In the majority of the cases, urobilinuria is associated with an unusual amount of bilirubin in the blood.

3. Almost always when urobilin is found in the urine it is found in the blood also.

4. Very often one finds in the urine, at the same time with urobilin, a certain quantity of bile salts.

Bilirubin and urobilin are two substances, chemically near neighbors, which can be changed one into the other by various chemicals. There is only one variety of urobilin; in the fresh urine it exists as urobilinogen, a closely related pigment. One knows, too, that these pigments differ from bilirubin by their weak tinctorial power, by their lessened toxicity, and by their greater diffusibility. Clinically, we know that urobilin and bilirubin coexist in the urine and that frequently urobilin succeeds bilirubin, and *vice versa*. Knowing that, *in vitro*, one can transform bilirubin into urobilin one is forced to the conclusion that *in vivo* a similar conversion is possible. An endeavor has been made to prove the relation of urobilin to retention of true bile pigments in the organism. Gilbert and Herscher have shown indubitably that this fact is true. In those cases showing urobilinuria, the amount of bilirubin in the blood is notably higher than normal. Urobilinuria is then an index of cholemia, but not every cholemia is accompanied with urobilinuria. In catarrhal icterus, at the beginning, urobilin exists alone in the urine, then bilirubin appears at the period of the disease when the stools have assumed the characteristic color of no bile and the icterus is intense, the urine contains only bilirubin. When jaundice diminishes, urobilin reappears in the urine, at first associated with bilirubin and then alone. To repeat, when the cholemia becomes intense, urobilin disappears from the urine and is replaced by bilirubin. Gilbert admits that when the kidney receives a too large quantity of bile pigment to eliminate, it becomes in a



way stupefied, and loses its power of reduction. That is to say, when the bilirubin content of the blood becomes abnormally raised, urobilin appears in the urine, but when cholemia becomes too great, bilirubin succeeds urobilin.

Is it fair to attribute these phenomena to the kidney, asks Brulé? If the conversion of bilirubin into urobilin takes place in the kidney, one should find urobilin neither in the blood nor in the other humors of the body. Gilbert and Herscher admit that they find no urobilinemia in the majority of their cases. But the opposite is the case, for Hayem and a host of others have frequently found on spectroscopic examination, urobilin in the blood. Not only spectroscopically can it be found in the blood but chemically as well, and not only in the blood, but also in ascitic and pleural fluids, whenever there is urobilinuria. Brulé, with Garban, has found bile salts associated with urobilin in the urine, cholaluria (Chauffard), which proves the relationship of urobilinuria with biliary retention, which means in turn that in certain conditions, elements of the bile are being alike retained in the organism, the bile salts passing as such into the urine, the bilirubin, being liberated only after having been transformed into urobilin.

But it remains to explain why it is that in certain cases and not in others bilirubin can be transformed into urobilin. Brulé admits that the facts brought forward by Gilbert and Herscher are important and true, but he believes they permit of an interpretation other than that offered by these investigators. The appearance in the urine of urobilin at times and of bilirubin at others, depends upon the intensity of the cholemia; for example, in the course of infectious jaundice, bilirubin is found in the urine when the bilirubinemia is 1 : 1000, and when the figure is 1 : 15,000 it is replaced by urobilin, which goes to show that bilirubin can appear in the urine only when the blood figure is high. A parallel is found in glucose which is found of course, normally in the blood, but which is excreted in the urine only when the amount in the blood is above the threshold of the individual for sugar. There may be a certain quantity of bilirubin in the blood and there may be a considerable retention in the tissues without there being bilirubinuria. The organism combats this pigment impregnation in another way: it changes the bilirubin into less toxic and more diffusible pigments, namely urobilin and urobilinogen, which will be found in the urine. With larger amounts of bilirubin the threshold is passed and the pigment will appear, but some of the bilirubin will be converted into urobilin, and the organism defends itself by bilirubinuria and urobilinuria. When biliary retention is still greater the threshold will be passed and the factors of defense will be weakened, so that all the bilirubin which can be eliminated will be as bilirubin and there will be no urobilinuria, the latter appearing only when there is a diminution of the cholemia.

Thus, a strong bilirubinemia is necessary for bilirubinuria; in other words, the human organism has a high threshold for bilirubin. Although this is true also of the rabbit, it is not true in every species, for in the dog the threshold is relatively low, the slightest biliary retention being followed by bilirubinuria, despite the absence of any abnormal cholemia.

The dog is able to eliminate when it is retained in mild excess in the organism, and urobilinuria in this animal is a defensive process a most superfluous in nature. Furthermore, urobilinuria is feeble in the dog when under the same conditions it is intense in man, and far from preceding bilirubinuria, it accompanies it, and often appears only a day or two later. Admitting the threshold theory for bilirubin, is the threshold fixed in the same species or the same individual? Brulé believes that according to the underlying disease, bilirubinuria appears with various figures for blood bilirubin. It is argued that the renal state may affect urobilin and not bilirubin, and Achard, and others, are of the opinion that renal lesions can well interfere with the elimination of urobilin and of urobilinogen.

If we believe that urobilinuria is but an expression of bilirubin retention should we accept the conclusions of Gilbert and Herscher, who consider that "urobilin is not a sign of hepatic insufficiency, but is independent of the liver function, that when urobilinuria exists at the same time as hepatic insufficiency, it is a coincidence and not a question of cause and effect?" Brulé believes the above-named authors are in part correct, but their statements are too sweeping. The causes of biliary retention appear more complicated today than ever before. Icterus is no longer a sign of a definite lesion, namely, obstruction in the bile passages, but should be regarded as the result of a trouble which has interfered with some one or other of the complex processes which have to do with the biliary function. Biliary retention and its corollary, urobilinuria may depend upon three kinds of very different lesions: (1) Lesion of the liver; (2) lesion of the bile passages; (3) lesion of the blood.

1. Retention of bile is seen in hepatic disease, in general infections and in intoxications, and in all these conditions, urobilinuria is very commonly seen. It is not a particular pigment secreted by the diseased liver, but, as has been said, is but a sign of biliary retention, and in certain cases is a *true sign of hepatic insufficiency*. This term is defined by Brulé as meaning not always a grave lesion of the liver; the least functional hepatic disturbance, which may have, in a few hours, completely disappeared leaving no trace behind, suffices to cause biliary salts and urobilin to appear in the urine. Even a simple indigestion, or a mild infection (biliousness) is enough. Urobilinuria, although a sign of hepatic insufficiency, does not measure the degree, and not every case of hepatic insufficiency shows urobilinuria, as witness the disappearance of urobilin and the appearance of bilirubin in severe cholemia (infectious jaundice). There is then this paradox that in grave icterus where the insufficiency is at its maximum, urobilinuria, the sign of insufficiency, is absent.

2. Another variety of biliary retention is seen in cases of biliary obstructions. Such cases are much more rare than formerly supposed—choledochitis, angiocholitis, once considered to be the cause of infectious jaundice and of jaundice in cirrhosis, can no longer be incriminated. However, the obstruction due to calculus or to tumor is a condition causing retention. In these cases, urobilinuria is rarer than in hepatic lesions—obstruction of the biliary passages causes a brutal, intense



retention, so that the bilirubin threshold is soon passed and only bilirubin appears. However, when icterus from calculus is abating, it will be found that urobilinuria succeeds the bilirubinuria. In these cases it cannot be claimed that urobilinuria is a sign of hepatic insufficiency, it is here only a sign of biliary retention.

3. The third variety of icterus, that due to retention of pigment of hemolytic origin. When there is an abnormal destruction of red cells the hemoglobin set free can be converted into bilirubin outside the liver and despite the healthy state of that organ, the large amounts formed cannot be eliminated. In these cases it is important to remember that *only the bile pigments* are retained, bile salts and cholesterin being eliminated normally. Another important fact is that in the great majority of the cases, urobilin is found in large amounts in the urine, while bilirubin is absent. It would appear then that the urobilinuria is a direct product of the conversion of hemoglobin, but this is not true, although such a change can be observed *in vitro*. There is little doubt that the hemoglobin liberated by hemolysis is first transformed into bilirubin and then into urobilin. If it is not found in the urine it is merely a sign that retention has not been great enough to pass the threshold for bilirubin.

A new theory to arouse any interest must explain certain clinical facts that other hypotheses have not been able to explain, and Brulé now turns to the theories sketched at the beginning of this abstract. The *hepatic theory* of Hayem has been of great interest inasmuch as it has emphasized the relation of urobilinuria to hepatic insufficiency and even to hemolysis, but it makes of urobilin a special pigment secreted by the liver, when it can no longer secrete bilirubin. Facts, however, show that urobilin is a lower product than bilirubin and comes from the latter. Furthermore this theory failing to recognize the relation between bilirubin and urobilin is incapable of explaining why bilirubinuria replaces urobilinemia at a certain stage of jaundice.

The *enterohepatic* theory which has many adherents seems very seductive at first view. One of its principal arguments is the clinical fact, which Brulé insists upon, that at a certain point in icterus, urobilinuria disappears. At this time the feces become decolorized, and the conclusion is reached that the presence of bile pigments in the intestine is indispensable for urobilinuria. This is a coincidence and not causal, for, when the bile ceases to enter the intestine, the bile retention is at its height and the bilirubin threshold being passed, urobilinuria disappears and bilirubinuria is found. Furthermore, the relation between stercobilin and urobilin is not constant enough, if the enterohepatic theory were exact. Urobilin has been found in the urine when no trace of stercobilinogen has been detected in the feces. Finally, this theory should be definitely rejected because it does not explain the relation of urobilinuria to bilirubinemia, nor the coincidence of urobilin and bile salts in the urine, nor the hemolytic urobilinuria, which Fischler has been able to produce in a dog with a complete biliary fistula.

The *renal theory* of Gilbert and Herscher has been discussed and the advantages and disadvantages pointed out. It indicates admirably



the relation of bilirubinemia to urobilinuria but it does not recognize the very frequent relation of urobilinuria to hepatic insufficiency. It cracks at the well-known phenomenon of urobilinemia. Urobilin is not formed at the kidney, it arrives there *preformed*, the change from bilirubin having been already effected in other tissues.

The *histogenic theory* is true enough but to be complete it must show why the conversion of bilirubin into urobilin is not constant, and must show how the theory explains the various causes of pigment retention.

The *hemolytic theory* is likewise true enough but it is applicable only to a limited number of cases.

Urobilinuria having been thus discussed, it remains for the clinician to know exactly what practical value it possesses. Brulé believes that is the best means of determining abnormal retention of bile pigments. Putting aside those cases of physiologic urobilinuria corresponding to Gilbert and Herscher's physiologic cholemia, urobilin is never found in health. It appears only when the bile pigments in the blood exceed the normal. It has been suggested to determine the amount of bilirubin in the blood which should be a better index of the degree of the cholemia than is urobilinuria. Such a suggestion does not take into consideration the fact that urobilinuria is seen when there is no cholemia. This is easily explained, for if bilirubin is retained in small quantities it can be rapidly converted into urobilin and eliminated as such without accumulating in the blood. Brulé calls attention to the importance of examining for other bile components than pigment, and the reader is referred to another article by Brulé reviewed elsewhere in this monograph where his views on dissociated bile retention are given. If urobilin and bile salts are tested for in the urine, one can absolutely define the cause of the biliary retention. If there is *an obstruction* in the bile passage, bile pigments (bilirubin and urobilin) and bile salts appear simultaneously in the urine—the *icterus will never be found dissociated*. When the retention is due to a *lesion of the liver cell*, all the elements may be retained parallelly, but they may be dissociated, either the pigments or the salts being retained, and in this case, one can be certain that there is no obstruction, for dissociated retention presupposes the intervention of a gland cell, like the liver cell, which alone is capable of selecting and choosing from among the bile elements. In the third class of cases, *hemolytic jaundice*, the icterus will be dissociated and only bile pigments will be found.

Study of urobilin and bile salts should not be made only in icteric or subicteric individuals—urobilinuria has been found when the cholemia is normal, and in these cases the bilirubin does not accumulate in the blood or in the tissues, and there is no jaundice. A systematic examination of the urine can alone show latent biliary retention which, according to Brulé and Garban, is very important. One can find it in nearly all liver conditions (alcoholic cirrhosis, tuberculous liver, chronic passive congestion, etc.) in infections and intoxications which injure the liver (pneumonia, typhoid fever, septicemia, appendicitis, chloroform or ether anesthetics, pregnancy, alcoholism, etc.). Often this mild biliary retention is the only sign that the liver is affected, showing hepatic

insufficiency in much the same way as the so-called febrile albuminuria in the course of pneumonia or typhoid fever shows the strain on the kidneys. In the majority of these latent bile retentions, the liver cell is affected, but in other cases there will be a hemolytic process, in which case examination for bile salts will be of the greatest importance.

**Urobilinuria with Cholelithiasis.** Hansen<sup>71</sup> found urobilinuria in 80 per cent. of fifty persons with cholelithiasis and in 100 per cent. of the thirty-three examined during gall-stone colic, while the findings were negative in 71 per cent. of 175 control cases. The mere presence of gall-stones is not enough to induce urobilinuria, but the latter is constant during an attack of gall-stone colic if the common bile duct is permeable. If the gall-stone has obstructed the common bile duct so that no bile is able to pass into the bowel, then bile pigment may be found in the urine, but no urobilin. In some of the cases which seemed to be gall-stone colic, but not urobilin was found in the urine, the reliability of this test was confirmed by the operation which disclosed duodenal ulcer, cancer of the liver or other lesion but no gall-stones. Of course, urobilinuria is not a specific reaction to cholelithiasis, but it is proving, in connection with other findings, a very valuable aid in the diagnosis and in the estimation of the course of the case with gall-stones. He theorizes to explain why gall-stone colic is accompanied by this abnormal insufficiency, a flooding of the liver with urobilin. One of his charts shows urobilinuria of 1 : 40, then 1 : 80 the first and second days of the attack, and then a gradual decline the four following days to zero. If the urine had not been tested until the fourth or fifth day, the urobilinuria would have escaped detection. His tests showed further that fever in itself does not induce urobilinuria. His improved technic for estimation of the urobilin content of the urine was described in the *Journal of the American Medical Association*, March 23, 1918, p. 896. He says it is far more sensitive than the Schlesinger reaction. The latter is positive when the response is within normal range.

An article dealing with the study of bile pigments in pernicious anemia is published by Schneider.<sup>72</sup>

**Jaundice.** When the clinician is confronted with a case of jaundice he should put two questions to himself—what is the causative agent of the icterus? by what mechanism is it causing biliary stagnation? The first question concerns the etiology, the second has to do with the physiopathology. The latter is the title of Brulé's paper.<sup>73</sup>

(a) *Hemolytic Icterus.* It is now generally admitted that in cases of this kind, whether congenital or acquired, jaundice is the result of excessive and continuous destruction of red blood cells and Brulé offers as proof: jaundice and anemia paralleling one another, existence of iron pigment in the organs, good results following iron therapy and experimental reproduction of the disease by hemolyzing agents. Therefore the hemoglobin liberated in excess is changed into bilirubin, but how does jaundice result? Some believe, because of the hyperproduction

<sup>71</sup> Abstract, *Journal of the American Medical Association*, 1920, lxxiv, 1614.

<sup>72</sup> *Journal of the American Medical Association*, 1920, lxxiv, 1759.

<sup>73</sup> *Bulletin médical*, 1919, lxxxiii, 709.



of bile pigments, that the bile becomes thick, pleiochromic and engorges the biliary canals, giving the picture of the usual retention type of icterus. Brulé takes exception to this view, and has found the bile in just such a case extremely labile; furthermore, if the jaundice were of the retention type then all components of the bile should be retained, whereas, in hemolytic icterus, only the bile pigments are held back, bile salts and cholesterin being retained scarcely at all. Bile pigments are in excess because they alone are formed from the hemoglobin, but where does this transformation of hemoglobin into bilirubin take place? Brulé believes the metamorphosis occurs in all tissues as well as in the liver, quoting Langhans, Quincke, Froin, as having observed extravasation of red cells under the skin and having then witnessed the development of bilirubin, extra-hepatic bile pigment formation. Thus hemolytic icterus is really not a disease of the liver at all, but a blood disease pure and simple.

(b) *Icterus Due to Lesions of Liver Cells.* Brulé believes with Abrami and others that lesions of the liver may be descending in origin and not dependent upon an ascending infection from the gall-bladder, and may exist without any evidence of angiocholitis. This hepatitis due to a descending infection he has reproduced in guinea-pigs. A typical cellular degeneration of the liver is seen, of course, in certain poisonings, notably in phosphorus and chloroform, in both of which involvement of the biliary channels is absent. In cirrhosis (Hanot) it has long been thought that jaundice is due to obliteration of the bile canaliculi by a chronic angiocholitis, but recently enough evidence has been brought forward to prove that this is not always the case, but that the primary lesion is in the parenchyma. In alcoholic cirrhosis the same state of affairs exists. Pathologic anatomy has shown that in infectious jaundice, and in icterus due to hepatic disease, the bile passages are frequently unaffected, but that there do exist lesions of the liver cells. In the condition called dissociated icterus, it has been shown that bile is dissociated and that but one bile element is retained, sometimes a salt, sometimes a pigment. In an abstract in the *Journal of the American Medical Association*, 1920, lxxiv, 987, such studies are recorded.

(c) *Icterus Due to Biliary Retention.* Brulé's observation on the physiopathology of jaundice have not only a theoretical interest, but also a therapeutic interest. Before hemolytic jaundice was recognized, many of such cases were being operated upon in the belief that the cause of the jaundice was obstructive, and much harm was done which could have been avoided. The recognition of dissociation in bile retention enables one to differentiate between Hanot's cirrhosis on the one hand, and icterus due to stone or cancer on the other. In other cases, one can distinguish between stone and infectious jaundice, between angiocholitis and septicemia with hepatic disturbance and lesion. Finally, if one will admit that the great majority of infectious jaundice cases act on the liver and not through the intervention of the bile ducts, therapy may be judiciously applied. One cannot, in severe icterus, expect drainage to help if the defect is in the cells of the liver, nor can he expect much from cholagogues which only cause contraction of the gall-bladder, if the flow of the bile is interfered with higher up, even in the liver itself.



**Dissociated Elimination of Elements of the Bile.** Waldrop classifies the different forms of jaundice from complete or partial retention of all the elements of the bile and the jaundice with isolated retention of bile pigments or of bile salts. Hemolytic jaundice is the perfect type of the latter group, but it includes also catarrhal jaundice in the active stage, and some cases of jaundice from cirrhosis, or from infectious or toxic disease of the liver; it may possibly include likewise the early phases of the other group. With alcoholic cirrhosis there may be no sign of toxic retention, as manifested by pruritus and bradycardia, but the blood dust is scanty, and the Hay and Pettenkofer reactions are usually positive. Intercurrent infection or abuse of alcohol or other toxic action is liable to induce a phase of exaggerated retention and hence augment the jaundice temporarily. Brault and Garban investigated for retention of bile in long series of patients, and found it in some persons who gave no evidence of jaundice but had tuberculous, malarial or other form of liver disease. In typhoid, also, there may be retention of bile salts, with urobilinuria, as also in pneumonia in male adults, and in all persons with chronic poisoning from any cause. Brulé warns that retention of bile elements with appendicitis suggests that the liver is vulnerable, and hence should not be subjected to the strain of chloroform. The bile salts are also liable to be retained during pregnancy, the retention increasing as the pregnancy progresses, and ceasing after delivery.

The clinical importance of recognizing this type of jaundice lies in this; that knowing there is dissociation of the bile one can say definitely there is a hepatic lesion and that the existing jaundice is not due to biliary obstruction. Brulé lays weight on the detection of urobilin, which is often found in early lesions of the liver without any jaundice—functional disturbance of the liver, "latent retention."

**Catarrhal Jaundice.** Lyon<sup>74</sup> applies his method detailed under gall-bladder disease, to the treatment of this condition. The present conception of catarrhal jaundice is, that it is due to an infection upward from the duodenum causing swelling and congestion of the common bile duct, with an increased production of mucus plugging up the ampulla of Vater. Lyon makes no mention of his method of diagnosing jaundice as does Brulé.

At the first visit, the possibility of antecedent mouth or respiratory tract infection is ascertained, then a study is made of catarrhal or infective processes in the stomach and duodenum by examining both fasting and digesting secretions from both of these zones. Among the bacteria recovered were streptococci, staphylococci, micrococcus catarrhalis and pneumococci in both the stomach and duodenum. All patients were cautioned against swallowing saliva, noses were sprayed with Dobell's solution, throats gargled with solution of permanganate of potassium, one grain to the ounce. The stomach was washed with liquor antisepticus alkalinus (in the hyperacid cases) and with hydrochloric acid solutions (in the subacid cases), then with water until the

<sup>74</sup> American Journal of the Medical Sciences, 1920, clix, 503.

washings were clear. Then 250 c.c. of solution, one day of potassium permanganate (1:8000) and the next day silver nitrate (1:20,000, 1:10,000) were introduced into the stomach and after remaining there five minutes, syringing out of the remainder was done. A duodenal tube was then passed and after the contents had been aspirated for study (see article by Lyon quoted above for details) magnesium sulphate is introduced and aspiration practiced. The A bile (that from the common duct) was found to be abnormal, the B bile (gall-bladder) also, but no bacteria in either one. (I can find no mention of the C bile, or bile from the liver itself in Lyon's work). Treatment should be given every day until the bile duct has been freed, and thereafter every second to fourth day. Following the biliary drainage, the duodenum is disinfected with permanganate or silver nitrate in amounts of 100 to 200 c.c. of the strength stated above. The solution remains for five minutes and is then aspirated (as much as 50 per cent. can be recovered), but no harmful effects have been seen from strengths and amounts such as are used by Lyon.

In the severe cases thus treated, the average duration of jaundice was seventeen days, the shortest being eleven, and in a group of cases treated by the expectant plan the average was thirty-five days, a reduction of over 50 per cent. Not only is the duration of the disease shortened, and the symptoms more promptly ameliorated, but the future dangers of drainage to the biliary apparatus, from static or infected bile from over-distended and consequently, atonic gall-bladder, are to a proportional extent avoided. Ousley<sup>75</sup> has practised duodenal lavage using sodium bicarbonate, sodium sulphate, each two drams, sodium salicylate, one dram in a liter of water, followed by 15 c.c. of a 20 per cent. solution of argyrol, and this treatment he gives every other day.

**Gall-bladder Disease.** In a preliminary report of a new method of diagnosing and treating diseases of the gall-bladder and biliary ducts, Lyon<sup>76</sup> acknowledges his debt to S. J. Meltzer whom he quotes as follows: "In experiments with magnesium sulphate, I observed that the local application of a 25 per cent. solution of that salt on the mucosa (of the duodenum) causes a completely local relaxation of the intestinal wall. It does not exert such an effect when the salt is administered by the mouth, that is, when it has to pass through the stomach before it reaches the intestines. The duodenal tube, however, apparently has reached an efficient practical stage. I make, therefore, the suggestion, to test in jaundice and biliary colic the local application of a 25 per cent. solution of magnesium sulphate by means of the duodenal tube. It may relax the sphincter of the common duct and permit the ejection of bile, and, perhaps, even permit the removal of a calculus of moderate size wedged in the duct in front of the papilla of Vater. Twenty-five c.c. of the solution as a dose for an adult will bring no harm. For babies, the dose should not exceed 4 c.c. The procedure could be developed into a practical, useful method."

In an extensive experience in the Navy, and in civilian practice, Lyon

<sup>75</sup> Southern Medical Journal, 1919, xii, 597.

<sup>76</sup> Journal of the American Medical Association, 1919, lxxiii, 980.



says he has proved that Meltzer's assumption is correct, and that within two to fifteen minutes after instillation directly into the duodenum of magnesium sulphate in various amounts and in various strengths, there is evacuation of bile into the duodenum. Magnesium sulphate appears to be a hormone which has the ability, not only to relax the common duct sphincter, and thereby drain the bile in the ducts, but also, simultaneously, to cause the gall-bladder to be compressed and to empty its contents. His studies have convinced Lyon that he can segregate bile from the ducts, gall-bladder and liver, and thus one is enabled to make a differential diagnosis between cholecystitis, cholelithiasis and choledochitis, in a scientifically accurate manner.

*Method of Aspiration.* The patient is examined fasting, after having rinsed the mouth with a solution of potassium permanganate one grain to two ounces of water, followed by a rinse with a weak solution of zinc chlorid (strength not given!). A sterile duodenal tube is passed and the fasting gastric residuum is aspirated and studied for acidity, bile and occult blood. Microscopically, attention is given to endogenous epithelium, polynuclear leukocytes, and to the bacterial flora, differentiating between endogenous and exogenous organisms. The stomach is then thoroughly rinsed and the patient is given a glass of water to drink while *slowly* swallowing the tube to the duodenal point, and while lying on the right side, with a pillow or sandbag elevating the hips.

The tube passes into the duodenum within fifteen to forty-five minutes, and this fact can be determined by the duodenal "tug," the character of the aspirated fluid, and the failure to recover material swallowed (broth, water).

Occasionally, difficulty is encountered by spasm, which can be overcome by injection of atropin, or by the use, for several days, of belladonna or benzyl benzoate. Once the tube is in the duodenum, a barrelful of air is introduced from a one ounce syringe, a connection is made with the *first* sterile aspirating bottle and gentle aspiration is begun.

Under normal conditions the duodenal contents should be bile-free (sphincter closed), pearly gray, and of syrupy and stringy consistency and should have a relatively small amount of flocculent or flaky sediment. When bile is grossly visible, there is a disturbed physiologic condition or a pathologic lesion of group organs physiologically related to this intestinal zone. The first bottle is detached and its contents examined bacteriologically, cytologically and chemically. From 50 to 100 c.c. of a sterile 25 per cent. magnesium sulphate is now introduced by a syringe or by gravity, and the tubing is connected with a *second* sterile bottle. Within two to ten minutes, bile is recovered, staining light yellow the magnesium sulphate still in the duodenum. When the color deepens to a pronounced yellow, the material in the second bottle is decanted into a sterile glass container, the bottle is reattached, and drainage is continued.

Flow of bile is intermittent, the first bile recovered is from the common duct because it is lighter yellow, more transparent, and much less mucoid than later bile. The first bile may be from 10 to 20 c.c. in amount, and



may require from one to three minutes to aspirate, when a sudden transition appears (seen first in the glass window of the tube) and this bile becomes darker, more viscid, more of a molasses color, and in normal gall-bladders is transparent. This bile, Lyon believes, is from the gall-bladder, and when it appears the second sterile bottle is detached and a *third* one is used, into which the bile is allowed to flow until all of this darker bile (more viscid, transparent or turbid), has been collected, and is being replaced by a lighter yellow, thinner and usually transparent bile, which is aspirated more slowly and intermittently, and which is the bile from the liver. This bile is collected in a fourth sterile bottle. Each portion is separately examined.

The bile from the gall-bladder varies from 30 to 100 c.c., the high normal should not exceed 75 c.c. In pathologic states of the gall-bladder these types are seen:

A. *Choledochitis*. The bile is more viscid, with an excess of flaky mucus, is turbid and usually "off" color; it contains pus cells enmeshed in mucus, epithelial cells and occasionally erythrocytes; cultures may show pathogenic organisms.

B. *Cholecystitis*. In cholecystitis without choledochitis, the first bile is relatively normal, grossly and cytologically and does not contain pathogenic organisms. The second bile is grossly pathologic—it is more viscid, it is turbid, with a flaky or stringy mucus, contains pus cells, red blood cells (occasionally) and desquamated epithelium, and cultures show pathogenic organisms (streptococci of various strains, staphylococci, *B. pyocyaneus*, *B. typhosus*, and *M. catarrhalis*). The viscosity, color and general appearance of the bile will, in pathologic conditions of the gall-bladder, suggest the diagnosis. The color varies from a deep golden yellow to a dark molasses yellow, transparent or turbid; to a light, mustard yellow, always turbid, and occasionally streaked with slimy mucus or a greenish mucus; to various shades of green or greenish black, and in one case, was of such a tarry consistency as to make aspiration slow and difficult.

C. *Cholelithiasis*. Evidence is found of cholecystitis, but the bile is gritty or sand-like in consistency, which microscopically is made up of crystals of bile salts. Lyon has found no case of pure hepatic infection.

Considerable success has been achieved in the treatment of cholecystitis, choledochitis, catarrhal jaundice and infective duodenitis by this direct medical drainage of the biliary apparatus and by direct disinfection of the duodenum and intestine by germicidal solutions.

The paper by Rolleston<sup>128</sup> which I am placing under this heading bears the title "Dyspeptic and other Referred Symptoms Associated with Disease of the Gall-bladder and of the Appendix." The author speaks almost synonymously of gall-bladder and appendix and I have preferred to place this abstract of Rolleston's paper under the above heading rather than under the section devoted to appendicitis.

**Mechanism of the Production of Symptoms.** 1. *Reflex*. Irritation in the appendix or gall-bladder may cause hypertonus of the stomach and

<sup>77</sup> British Medical Journal, March 6, 1920, p. 317.

spasm of, or failure to relax on the part of, the pyloric or ileocecal sphincter, leading to gastric or ileal stasis. (See Gastric Hypermotility.) Moynihan has seen vigorous contraction of the stomach during the course of operations for appendix dyspepsia, and the pyloric spasm or failure to relax has been considered as a protective mechanism. The epigastric pain has received much consideration. Mackenzie maintains that it is in the peripheral termination of the sixth and seventh dorsal nerves in the abdominal wall, and that this depends on the irritated focus in the spinal cord, but Hurst claims that the pain is visceral, in the pyloric end of the stomach, and due to the peristalsis. Both agree, however, that the tenderness is due, not to pressure on the stomach, but to the irritated focus in the spinal cord, which carries an exaggerated sensory effect when the skin, and especially the muscle and the underlying subperitoneal tissues, are pressed on.

2. *Mechanical.* Adhesions (pericholecystic) may embarrass the movements of the stomach, interfere with the passage of food through the pylorus, or even lead to an hour-glass stomach, while periappendicular adhesions may cause stasis and toxemia.

3. *Toxic.* Absorption of toxins from gall-bladder or appendix may set up toxemia, cause myocarditis, and damage the mucous membrane of the stomach and intestines, causing hemorrhage. The above train of effects is probably more common from the gall-bladder than from the appendix.

4. *Infective.* Organisms from appendix or gall-bladder may infect the kidneys, especially the right. Infection of the gall-bladder is prone to spread to the pancreas, and local thrombophlebitis of branches of the iliac veins, secondary to appendicitis, may give rise to small pulmonary emboli and pleurisy. Malignant endocarditis has been found to be associated with gall-bladder infection. Although both the gall-bladder and appendix are often associated in the infection, it is probable that most commonly the appendix is the earlier affected and that from this focus the gall-bladder is invaded.

**DYSPEPSIA.** The term "surgical dyspepsia" is frequently used, since many cases of dyspepsia resisting medical treatment, disappear, when operative exploration has revealed the existence of an organic lesion. One must not conclude, however, that all dyspepsias require operation. It is far more important, says Rolleston, for medicine to prevent infection of the gall-bladder and appendix by attention to potential foci of infection—stomach, teeth, tonsils, food. The dyspeptic symptoms associated with chronic disease of the gall-bladder or appendix vary so that it is sometimes impossible to tell whether the gall-bladder or appendix is at fault. Furthermore, there may be such a close mimicking of ulcer that the diagnosis is extremely difficult. In 1078 cases of gastric and duodenal ulcer at the Mayo clinic, 40 per cent. showed disease of the appendix and 9.7 per cent. disease of the gall-bladder.

In the differential diagnosis between appendix and gall-bladder dyspepsia on the one hand, and gastric and duodenal ulcer on the other, Rolleston believes that the *x*-ray is of the greatest value. He quotes Hurst as laying weight in appendix dyspepsia on the presence of adhe-

sions, ileal and cecal stasis, and although hypertonus of the stomach may be present, it is much less frequent and less well marked than in duodenal ulcer. Spriggs, whose work with illustrations received full consideration in last year's *PROGRESSIVE MEDICINE* (p. 87), claims a great deal for the *x-ray* diagnosis of appendicitis. Adhesions around the gall-bladder are characterized by a high position of the stomach, displacement of the pylorus to the right, distortion of the duodenal cap and of the hepatic flexure of the colon, and six- to eight-hour retention.

Turning to other means of diagnosis, it should be remembered that the pain of gastric ulcer is relieved by food and alkalis and in duodenal ulcer there is usually complete freedom from symptoms and hyperchlorhydria. In both conditions occult blood, he states, is much more apt to be present in the feces than in referred dyspepsias. In favor of appendicitis are radiation of pain toward the right iliac fossa, with local tenderness there or on rectal examination, and Bastedo's sign. Deep tenderness to the right of the spine between the seventh and eighth ribs is regarded as pathognomonic of pericholecystitic adhesions by Friedmann who considered it of more value than the *x-rays*.

*Chronic colitis* is occasionally due to continued infection from the gall-bladder or appendix.

*Glycosuria and diabetes* may be due to pancreatitis, secondary to infection from a gall-bladder.

*Cardiac Symptoms.* Palpitation, irregularity and substernal distress may be associated with the referred dyspepsia, while absorption of toxins from an inflamed gall-bladder or ducts may cause myocarditis, anginoid symptoms and cardiac failure.

*Pyelitis and pyelonephritis* may be due to infection with *B. Coli*, either from the gall-bladder or from the appendix, and is usually seen in the right kidney.

*Synovitis and Arthritis.* Appendicitis and cholecystitis rarely cause these conditions, but some years ago, Poynton, in discussing the association of appendicitis with arthritis, came to the conclusion that the articular affection was probably secondary to the appendicitis.

Smithies<sup>78</sup> presents an analysis of 1000 operatively demonstrated cases of gall-bladder disease.

*Sex.* Females, 672; male; 328 (ratio 2.05 : 1).

*Age.* Average age, 43.2 years—females, 41.9; males, 44.5. The minimum age was in females, 13 years and in males 15 years. The maximum was 76 for each sex. Table I shows incidences of sex in gall-bladder disease.

#### FEMALES.

	Cases.	Per cent.
Under 20 years . . . . .	12	1.8
20 to 30 years . . . . .	118	17.6
30 to 40 " . . . . .	169	25.2
40 to 50 " . . . . .	183	27.2
50 to 60 " . . . . .	121	18.0
60 to 70 " . . . . .	60	8.9
Over 70 " . . . . .	9	1.3

<sup>78</sup> Northwest Medicine, 1920, xix, 31.



MALES.		Cases.	Per cent.
Under 20 years	. . . . .	2	0.6
20 to 30	" . . . . .	41	12.5
30 to 40	" . . . . .	75	22.9
40 to 50	" . . . . .	85	25.9
50 to 60	" . . . . .	85	25.9
60 to 70	" . . . . .	34	10.3
Over 70	" . . . . .	6	1.8

Table II shows the relationship of bacteremias, septicemias, etc., to gall-bladder disease.

	Cases.	Per cent.
Typhoid fever . . . . .	206	20.6
Measles . . . . .	180	18.0
Chronic tonsillitis . . . . .	146	14.6
Scarlet fever . . . . .	145	14.5
Pneumonia . . . . .	115	11.5
Infected teeth . . . . .	93	9.3
Chronic rheumatism . . . . .	92	9.2
Malaria . . . . .	87	8.7
Whooping-cough . . . . .	75	7.5
La grippe . . . . .	66	6.8
Mumps . . . . .	62	6.2
Diphtheria . . . . .	47	4.7
Chicken-pox . . . . .	47	4.7
Chronic sore-throat . . . . .	46	4.6
Chronic bronchitis . . . . .	20	2.0

Table III shows summary of findings at laparotomy.

	Cases.	Per cent.
Cholecystitis with stones . . . . .	509	50.9
Cholecystitis with "sandy bile" . . . . .	46	4.6
Carcinoma with stones (14) . . . . .	19	1.9
Carcinoma without stones (5) . . . . .	...	...
Cholecystitis without stones . . . . .	434	43.4

#### ASSOCIATED LESIONS.

	Cases.	Per cent.
Appendix diseases . . . . .	682	68.2
Gastric ulcer . . . . .	43	4.3
Duodenal ulcer . . . . .	37	3.7
Gastric cancer . . . . .	14	1.4
Pancreatitis (acute 2) . . . . .	65	6.5
Pancreatitis (chronic 63) . . . . .	...	...
Enlarged lymph glands . . . . .	137	13.7
Non-malignant . . . . .	124	12.4
Malignant . . . . .	13	1.3
Liver enlarged . . . . .	73	7.3

CLINICAL SYMPTOMATOLOGY. There were 59 cases of gall-stones in which there were no disturbances that pointed to gall-bladder upset. Smithies found the typical obese or fatty inclined person to be represented in only 8 per cent. of his series. *Belching* was prominent and distressing in 68.9 per cent., and was commonly associated with pyrosis or water brash. *Nausea* was annoying in 37.6 per cent. *Appetite* was styled good in 36.3 per cent., pain in 35.3 per cent. and poor in 27.3 per cent. *Bowels*. There was no anomaly in 28.2 per cent., constipation in 61.2 per cent., persistent diarrhea in 5.1 per cent., and alternating

diarrhea and constipation in 4.4. per cent. Persistent diarrhea was the presenting symptom in 8 of the malignant cases. *Pain* was a characteristic symptom in 95.5 per cent., it was intermittent in 68.8 per cent. and constant discomfort or actual pain in 21.1 per cent. The main characteristic of the pain is that it appears irregularly in an individual previously well or it occurs constantly without any apparent causative factors, the characteristic being in marked contrast to the pain of gastric ulcer. (See Moynihan—Gastric Ulcer). The severe colics are usually described as knife-like, stabbing, piercing, doubling up or boring pain. If not colicky in nature it is described as a sensation of fullness, up-pressure, soreness, dull ache, burning. The pain is in the right upper quadrant in 74 per cent., and throughout the entire epigastrium in 14 per cent. In 4 per cent. the pain lay in the back either at, or beneath, the scapulæ or along the spine, from the eighth to the twelfth dorsal vertebrae. In 5 cases all the pain was to the left of the mid-line either in the abdomen or beneath the left scapula. There were two patients in whom disease of the right hip-joint was suspected because of more or less constant pain in that joint. There was no transmission of the pain in 32 per cent. of the cases. In 23 per cent. of the stone cases, there was no transmissible distress, while in 41 per cent. of the instances of non-calculous cholecystitis there was no radiation of pain. When transmitted, it was usually into the right back or infrascapular zone (63 per cent.). In 12 per cent. the radiation was under the right ribs, in 7 per cent. toward the sternum, midepigastrium, the left scapular or the left rib edge. In 4 per cent. there was definite radiation of pain constantly to the region of the navel.

*Abdominal tenderness* was recorded in 833 cases; there was no abdominal tenderness in 11.7 per cent.; there was dorsal tenderness in 4 per cent. of 760 cases specifically examined for this. *Epigastric* tumor or ridge was present in 8.9 per cent. and the liver was palpable in 3.9 per cent. *Jaundice* was seen in 28.7 per cent.; the stools were clay colored in 18.1 per cent.; excess of bile pigment in the urine was found in 19 per cent.

*Vomiting* was an annoying symptom in 45.2 per cent. Gastric achylia was seen in 20.9 per cent. In 21 per cent. of 87 cases of cholelithiasis gall-stones were diagnosed by *x-ray*.

**Achylia in Gall-bladder Disease.** Fravel,<sup>79</sup> after quoting many authorities who emphasize hyperchlorhydria in gall-bladder disease, with and without, stones, states that of 61 cases of bile-tract infection, 16 showed an absence of free HCl, 45 showed free acid of less than 20, 11 were within the bounds of normal and only 5 exhibited increase of free HCl. Referring to the total acidity, 11 cases had 50 or more, and 39 showed an acidity of less than 40. I am unable to make the author's figures add up to 61, the number of cases reported, as in one instance they total 77 and in the other 50. The discrepancy is unexplained.

The writer says hypo-acidity may be the result of loss of a hormone secreted by the normal gall-bladder, or it may be due to a disturbance

<sup>79</sup> American Journal of the Medical Sciences, 1920, clix, 512.

of intermediate chlorid metabolism. The pain is due to increased intra-gastric pressure, although pylorospasm may occur in hypo-acidity.

Rydgaard<sup>80</sup> found achylia in 47.4 per cent. of Rovsing's operative gall-stone cases, and in 52 per cent. of a total of 471 cases compiled, including the Rovsing cases in 26 men and 132 women. The sex and age do not seem to influence the achylia, but 74 per cent. of the 135 patients with stones obstructing the cystic duct had achylia or hypo-achylia. In some cases the achylia developed as the cystic duct became obstructed, showing the special dependence of the former on the latter. It seems plausible to assume that the incontinence of the sphincter papillæ, which is so often entailed by the stretching of the cystic duct by the gall-stones, upsets the physiologic process of the neutralizing of the acid stomach content by the bile. The former is poured out unneutralized into the duodenum, and the irritation of the duodenal wall from its acidity sets up reflex action which entails the achylia. When the sphincter is normal, there is no achylia, notwithstanding the presence of gall-stones. Other arguments are presented which sustain Rovsing's conviction that the gall-bladder is a physiologically important organ, and that it should not be removed without imperative indications for this. Cholecystotomy is all that is necessary in many cases to cure both the gall-stone disturbances and the achylia. Even if there should be recurrence of stones, this is not enough of a reason for removing the gall-bladder, any more than the kidney under similar conditions. The experiences related and the theoretical reasoning all emphasize the necessity for early operative measures in cholelithiasis, getting rid of the stones before the cystic duct has been stretched to a degree that entails incontinence. An early operation also wards off achylia and, in warding this off, prevents infection. As soon as the first symptoms warn of the presence of gall-stones, operative measures should be applied at once, Rydgaard reiterates in conclusion.

**Gall-stones.** Rowlands<sup>81</sup> believes that nearly all gall-stones are formed in the gall-bladder and are due to:

- (a) Infection of the gall-bladder.
- (b) Overconcentration of the bile.

(a) Infection may occur through the blood stream, through the lymphatics or ascend along the ducts from the duodenum, although infection by the blood stream is the most important. The most common organisms are the streptococcus, *B. typhosus* and *B. coli*.

(b) Four-fifths of the patients suffering from gall-stones are women who have had children and in them symptoms often date from the time of pregnancy, at which time the bile is very concentrated.

The cystic duct is very narrow, tortuous, and its mucous membrane is raised into valvular folds, so that it is very difficult for any but very small stones to pass through it. It is much narrower than any part of the common bile duct except at the latter's termination in the papilla, therefore the large majority of sufferers from gall-stones never develop jaundice. It is important to remember that the part of the common

<sup>80</sup> Abstract, Journal of the American Medical Association, 1920, lxxiv, 709.

<sup>81</sup> British Medical Journal, May 15, 1920, p. 665.



bile duct traversing the pancreas is not as easily distended as the first part of the duct, and it often happens that the common bile duct is shaped like a funnel and stones become impacted in the pancreatic portion of the duct. The duodenal papilla is very narrow, and stones become arrested here which are able to pass freely through the other portion of the duct, and when impacted at this point damming back of bile and pancreatic juice occurs.

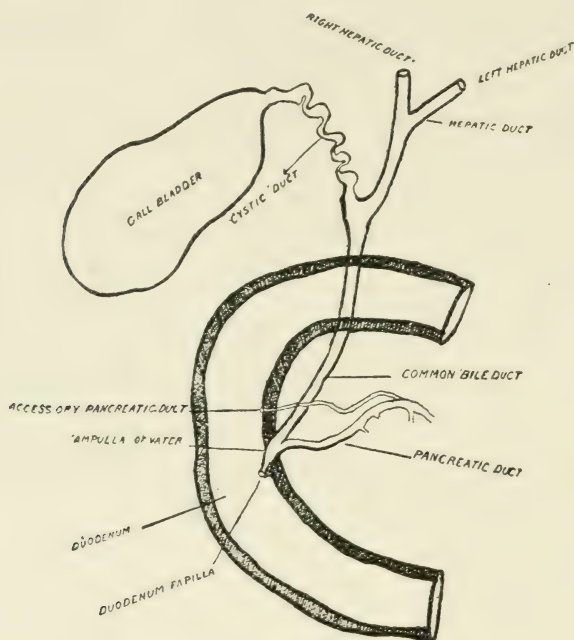


FIG. 14.—Anatomy of the biliary apparatus.

**SYMPTOMS.** 1. *Stones in the gall-bladder* may cause (a) recurrent attacks of pain in the right hypochondrium associated with vomiting and local tenderness. (Often mistaken for gastritis.) It may be possible to feel the gall-bladder during the colic or there may be a "catch" on deep inspiration and tenderness on palpation. (b) Or a dull aching pain in the right hypochondrium and right shoulder, with a distaste for food and flatulent dyspepsia. No swelling is felt, unless there is obstruction of the cystic duct or cholecystitis with local peritonitis. No jaundice is seen unless the common bile duct is also obstructed.

2. *Stone in the cystic duct* causes colic at intervals with a swelling in the right hypochondrium, or even in the right iliac fossa. Jaundice is absent unless the stone is junctional, and presses upon, or otherwise obstructs the hepatic or common duct. When the stone falls back, colic is abated, but impaction is followed by suppuration and even sloughing, with perforation later. "It is still a common error to believe that gall-stones are unlikely without a history of jaundice, but it should be remembered that as the cystic duct is narrower than the common duct,

except at the papilla, more stones get impacted in the cystic duct than elsewhere, and that jaundice is really an exceptional and late sign of gall-stones."

3. *Stone in the common duct* usually causes colic and jaundice sooner or later and often fever due to cholangitis. Sometimes stones impacted in the common duct do not cause colic but only nausea. There is tenderness above and to the right of the umbilicus over the common duct.

DIAGNOSIS. (a) *Stones in the Gall-bladder.* Cholelithiasis gives rise to reflex symptoms in stomach and duodenum, and may simulate gastric or duodenal ulcer or chronic appendicitis. The absence of hyperacidity is against ulcer and in favor of stone. Blood in the stomach contents or feces speaks for ulcer, but Rowlands has seen profuse melena due to the erosion of the cystic artery by a gall-stone impacted at the neck of the gall-bladder. Anemia and wasting rarely occur with gall-stones but are commonly seen in ulcer.

The time relationship of pain to food is not characteristic. Local tenderness below the ninth right costal cartilage is much in favor of gall-stones. Rowlands believes that x-rays are of little value, since radiography does not often show gall-stones, a statement which will not be corroborated by Pancoast and Pfahler, to say nothing of Case and George.

(b) *Biliary Colic Without Jaundice.* The distribution of pain distinguishes it from right renal colic. Pancreatic colic is rare and the pain is mesial and lower down. Intestinal colic is a far more common source of error, but it is rarely so very violent as biliary colic. Appendiceal colic is rarely so severe, the pain is lower down, referred to the umbilicus, and there is tenderness over the appendix.

(c) *Biliary Colic with Jaundice.* Jaundice due to cholelithiasis must be distinguished from that due to other causes—cirrhosis, growth, hydatid cysts of the liver or pressure from contiguous growths. The absence of severe pain is in favor of catarrhal jaundice or chronic pancreatitis. Cancer with jaundice may cause severe pain but the colic is rarely so acute and abrupt as that due to stone, and the jaundice is gradual in its onset, progressive and severe, but not sudden, remittent or intermittent and moderate as it is with gall-stones. Long continued and black jaundice is very rarely due to gall-stones.

*Indications for Operation.* For obstruction of the cystic duct or neck of the gall-bladder which is not relieved within forty-eight hours, it is imperative to operate in order to avoid suppuration and its complications. Jaundice which is neither slight nor transient (not catarrhal) calls for early exploration. Sometimes it is advisable to wait a few days when there is fever due to exacerbation of existing cholangitis, for it is safer to operate in a quiet period. When gall-stones in the gall-bladder give rise to symptoms, such as repeated attacks of colic or localized pain with flatulent dyspepsia, operation is advisable to avoid complications, especially carcinoma of the gall-bladder. The mortality of operations for gall-stones has greatly diminished. From 1913–1915 inclusive, the Mayos had a mortality of 1.2 per cent. in 1767 cholecystec-

tomies. The mortality of choledochotomy in the absence of serious symptoms of infection or jaundice of long duration is about 2.5 per cent., but when infection of the bile ducts has occurred, with remittent fever and deep jaundice and infective cholangitis, the mortality is about 15 per cent. Duodencholedochotomy, for removal of stone in the papilla of Vater has a mortality of about 8 per cent., but it is a very severe operation and is apt to be followed by a duodenal fistula.

*Recurrence of Symptoms Following Operation for Gall-stone Disease.* From his rich experience, Deaver<sup>82</sup> finds that recurrence of symptoms is increasing. The pathologic conditions found in re-operations are:

	Cases.
Adhesions . . . . .	39
Stone in gall-bladder and ducts . . . . .	26
Cholecystitis . . . . .	17
Fistula . . . . .	11
Biliary . . . . .	9
Duodenal . . . . .	2
Common duct obstruction . . . . .	10
Chronic pancreatitis . . . . .	8
Pancreatic lymphangitis . . . . .	6
Cholangitis . . . . .	6
Pyloric obstruction . . . . .	5
Dilatation of ducts . . . . .	5
Common duct . . . . .	4
Cystic duct . . . . .	1
Carcinoma . . . . .	4
Pancreas . . . . .	2
Gall-bladder . . . . .	2
Stricture of the ampulla of Vater . . . . .	2

**The Stomach Mask of Gall-stone Disease.** Soca<sup>83</sup> emphasizes that the radiating pain from liver colic may extend to quite a distance, and at some of the remote points thus reached it may set up a set of secondary symptoms which are liable to mask the primary disturbance and mislead the physician. The most frequent and the most dangerous form is when the secondary phenomena occur in the stomach. Even experienced and cautious physicians often yield to suggestion in such cases as readily as a hysteric girl. The patient's statements deal only with the stomach, and his description of his symptoms may fit some well defined stomach affection. In short, Soca reiterates, when confronted with any painful stomach symptoms, do not pay any heed to the stomach until the liver can be definitely excluded. The phrenic and scapular tender points with biliary lesions are often misleading, as also the costal, the shoulder and the pancreaticoduodenal points. The gall-bladder may not be tender on superficial examination, but if the finger is dug in deep, and the patient is told to breathe deep, in the midst of the inspiration the patient stops it short and makes an exclamation of pain. Soca calls this the *signo del grito*, as the patient utters a cry. Another instructive sign is elicited by holding up the liver from below, placing the hand just below the ribs, as the patient takes a deep inspiration. The diseased liver thus is compressed as the diaphragm descends, and an intense pain

<sup>82</sup> Journal of the American Medical Association, 1920, lxxiv, 1061.

<sup>83</sup> Abstract, Journal of the American Medical Association, 1919, lxxiii, 233.



is felt throughout it. Soca has named this the "signo del torno" as the liver is thus held in a vise, as it were. He illustrates his remarks with numerous instructive case histories. One shows that pain in the scapular region, with nothing to be found in the pleura or lungs, should suggest liver disease. Periodical vomiting first gave the clue in some cases. In one case the liver colic took the form of typical tabetic gastric crises; in other cases the gastric mask simulated nervous motor dyspepsia or the clinical picture of simple gastric or duodenal ulcer. The gastric or duodenal pain of biliary origin may assume the true rhythmic type of simple ulcer for days at a time. Even hematemesis may occur from cholelithiasis alone. One woman of fifty-four nearly died from the recurring hematemesis but the stomach was found normal and the gall-bladder full of stones. Ingestion of bismuth may relieve the gastric pains even when they seem to be due exclusively to the biliary apparatus.

### DISEASES OF THE PANCREAS.

No better introduction to this section of PROGRESSIVE MEDICINE can be offered than the few prefatory remarks made by Sir A. E. Garrod in the Schorstein Lecture for 1920.<sup>84</sup>

"In point of diagnostic display the liver and the pancreas, both glands of many vital functions, may be compared to a shop window and an office door. Derangement of the work of the shop may be obvious to the passer-by in the street, whereas what goes on behind the ground glass of the office door is hidden from public view, and is only manifested in the indirect effects of disorder of the activities within. If only the pancreas produced such a colored secretion as the bile how much easier would be the diagnosis of many of its lesions. As it is, the position of the pancreas, sufficiently remote to shield it from examination, but not from injury, and the fact that its secretion is poured into so inaccessible a region of the alimentary canal, enabled it for a long time to puzzle the physiologist and to baffle the physician.

"In the middle of the last century, Sir Thomas Watson, in one of those delightful lectures of his which, in lucidity and literary style, rank with those of Trousseau, spoke as follows: 'It may seem a slight to the pancreas to pass it over without noticing the diseases to which it is subject. But really these diseases appear to be but few; and they do not signify their existence by any plain or intelligible signs.' Somewhat later, Bristowe, in his well-known text-book of medicine, expressed his belief that in the great majority of cases of pancreatic disease will doubtless remain undetected during life. But some other writers of that period struck a more hopeful note, and among them Wardell, who, in 1871, wrote, 'No symptoms are pathognomonic of pancreatic disease; an assemblage of symptoms indicates the probability of its lesions.' These words still hold true today, and they embody the thesis of this lecture.

"It is true that we have learned to recognize, in fat necrosis, a sign pathognomonic of certain lesions of the gland; but since this is only

<sup>84</sup> Lancet, April 3, 1920, p. 749.

made manifest by opening the abdomen it lends us no help at the bedside. One other sign has been claimed as distinctive—namely, true steatorrhea, which was recognized by Kunzmann as early as 1824, and independently by Richard Bright in 1832, as indicative of pancreatic disease. Even nowadays pancreatic lesions often escape diagnosis, and Paul Carnot puts his finger upon the cause of many such failures in the following passage: 'Le plus difficile est, souvent alors, de songer au pancreas, étant donné la rareté apparente des affections de cette glande.' The more constantly we bear the pancreas in mind as a possible seat of origin of obscure abdominal troubles the less likely shall we be to overlook its lesions."

Lastly, there are certain syndromes which experience has taught us to associate with pancreatic lesions; thus, carcinoma of the head of the pancreas is made upon purely clinical evidence, and in cases of bronzed diabetes with the enlarged cirrhotic liver and peculiar pigmentation, the pancreas is always implicated.

Garrod places the diagnostic indications in three main groups:

Physical signs and symptoms.	Defects of external secretion.	Defects of internal secretion.
Aspect . . . . .	Steatorrhea	Glycosuria.
Tumor . . . . .	Fatty stools	Lowered sugar tolerance.
Pain . . . . .	Creatorrhea	
Tenderness . . . . .	Impaired casein digestion	Cambridge's tests.
Cyanosis		
Vomiting		
Constipation . . . . .	Duodenal sound	
Diarrhea . . . . .	Einhorn's method	
Jaundice . . . . .	Oil breakfast	
Sympathetic . . . . .	Sahli's capsules	
Signs . . . . .	Schmidt's test	
Ocular . . . . .	Kashiwado's nuclear test	
Loewi's test	Sajodin test	
	Diastase test in urine and feces	

Speaking of laboratory tests, he says none is to be looked to for a penny-in-the-slot diagnosis. Taken by itself, each test may fail or actually mislead, and one must know his test well before he can estimate the significance of its answers. When there is so great a choice of tests, workers tend naturally to concentrate upon some few which have seemed to them especially useful and easy of application.

**Physical Signs and Symptoms.** In *acute pancreatitis* these are best seen although the large cysts produce far more conspicuous swellings, and the carcinomata more distinct pressure signs. Typical though the symptoms of acute pancreatitis are, the diagnosis is often wrongly made of acute intestinal obstruction. An enlarged pancreas forms a tumor in the upper part of the abdomen between the ensiform cartilage and the umbilicus. It does not move with respiration and has an ill-defined outline. In thin subjects the pancreas may be felt, but the dulness is obscured by the overlying stomach and intestine. Ewart claims that the size of the gland may be determined with considerable accuracy by percussion over the back.

The pain of pancreatic disease may be continuous or paroxysmal, and being felt in the abdomen is likely to be confused with other acute abdominal pains. Garrod lays particular emphasis on pain across the back. Vomiting is usually severe, cyanosis is present and obstinate constipation is the symptom leading to the false diagnosis of intestinal obstruction. Although the abdomen is usually distended there is less rigidity than in other acute inflammations within the abdomen.

Of pressure symptoms, jaundice is of great moment. In cases of carcinoma of the head of the gland, jaundice is of an extreme degree and complete absence of urobilin from the stools indicates complete occlusion of the bile duct. Of the slighter varieties of acute pancreatitis we have, with one exception, but little information, and the exception is the metastasis of mumps. Cammidge has found his test positive in 4 cases out of 8. Glycosuria is found, and transient steatorrhea has been observed. Garrod quotes the only autopsy in such a case, that of Lemoine and Lapasset, and in this instance the pancreas was swollen, edematous, congested and of a reddish gray tint.

Catarrhal jaundice has been thought to have its origin in a swelling of the pancreas (Oser and Mayo-Robson), with the absence of jaundice in almost all cases of the pancreatitis of mumps, is a strong argument against the connection of catarrhal jaundice with a catarrhal pancreatitis, and it is certainly no feature of cases of grave pancreatitis, hemorrhagic or other. Infection from biliary tract to pancreas is prone to occur, so another cause for jaundice apart from compression is to be considered. A tumor of the pancreas may cause obstruction of the duodenum and pressure upon the portal vein and vena cava.

Eye changes commonly seen in Graves's disease, have been observed. (Cohn and Peiser.) Of 5 cases, exophthalmos was found in 4, von Graefe's sign in 4, Moebius and Stellwag's sign in all 5, and also tremor and dermatography in all. Garrod has confirmed the report of Cohn and Peiser. If the eye symptoms are really due to excessive thyroid secretion, it is the sympathetic nervous system which is stimulating the gland to overactivity and this is not to be wondered at since the pancreas is a near neighbor of the great abdominal ganglia and plexuses. The severe and often paroxysmal pains, the vomiting and collapse are attributed by many to this proximity. There is evidence, furthermore, of a restraining influence which is withdrawn when the pancreas becomes diseased.

To test the existence of such a "soft pedal influence," as Garrod calls it, Loewi suggested his adrenalin mydriasis test. Two or three drops of a 1 : 1000 adrenalin are dropped into the conjunctival sac and repeated five minutes later. In a few cases, by no means all, there is conspicuous dilatation in the course of thirty to sixty minutes. The pupil is eccentrically dilated and oval. In Loewi's first series, mydriasis was seen in 1 of 3 cases of Graves's disease, and in 10 out of 18 diabetes. There were no gross cases of pancreatic disease in the series. Garrod has used the test extensively and believes it to be of undoubted value in the diagnosis of pancreatic lesions, provided that its ways have been studied and its limitations fully recognized. He has seen it, unlike



Loewi's experience, in only a very few cases of diabetes. Repeatedly there has been failure to obtain dilatation when the test is repeated, within a day or two, upon an eye which had previously dilated, whereas the mydriasis was again brought out after a longer interval. One must be certain that the iris is mobile, for Garrod has been deceived by trying to dilate a pupil fixed by synechiæ and dilatation is inhibited, too, by the administration of morphin.

The test may fail, at a later stage, in a case in which dilatation had occurred at an earlier period, and it may fail in a case of gross pancreatic disease and be present in another with an apparent normal gland. Despite these discouraging actions of the test, Garrod believes that when there is adrenalin mydriasis it is strongly suggestive of a pancreatic lesion, although he never ventures such a diagnosis upon this reaction alone—"of few of the tests of pancreatic efficiency can more be said." One of the drawbacks of the test is, that it is, if anything, too delicate and may give a reaction to a lesion which simply worries the pancreas without damaging it a great deal, but it has the advantage of being most marked at a stage when the excretory functions of the gland are not seriously impaired.

I shall insert here in the midst of the review of Garrod's paper, a brief report by Cockcroft<sup>85</sup> of two cases where this test was tried and where the clinical findings were controlled by autopsy. Both were cases where involvement of the pancreas might have been suspected, but in only one was there evident disease. In the first case in which the pancreas was completely free from disease and quite efficient, Loewi's reaction was completely negative on three separate occasions, while in the second case in which the pancreas was almost completely disorganized, the reaction was markedly positive, also on three separate occasions. But to resume with Garrod.

**The Indications of Abeyance of the External Secretion of the Pancreas.** True steatorrhea is almost pathognomonic of pancreatic disease and steatorrhea means the passage with the feces of liquid fat which solidifies on cooling. There are reasons for the belief that both the external and internal secretions of the pancreas take part in the utilizations of fats, the lipase being concerned with the splitting of fats, the internal secretion with their absorption. In the stools of a healthy man, some 75 per cent. of the fat is in a split form, whereas some patients with pancreatic disease pass as little as 20 per cent. in the forms of fatty acids and soaps. In true steatorrhea great importance is attached to the excess of fats in the stools, but of still greater importance is the undue proportion of neutral fat. When there is no gross steatorrhea the microscope may reveal abundant fat globules, and many fatty acid crystals. The gross appearance of the stools is justly described as elephantine.

The jaundice obscures to some extent the proper evaluation of the fecal fats, for absence of bile of itself causes a great impairment of fat absorption, but even when the pancreatic duct alone is blocked, divergent results are obtained. In the majority of cases there is no duct blockage

<sup>85</sup> British Medical Journal, May 15, 1920, p. 669.

and the impairment of secretion results from damage to glandular tissue, and is less in degree. A patient with grave disease of the pancreas may pass stools with normal fat content and this is true even of some cases in which the duct is obstructed, probably because the duct of Santorini remains patent and provides an emergency outlet. When there is a 40 to 50 per cent. proportion of fats in the dried feces it is strongly suggestive of pancreatic disease. It will be seen from the foregoing, that a patient whose pancreas is diseased may pass excess of neutral fats in his motions or a great excess of fats, fatty acids and soaps, without any undue proportion of neutral fats. Lastly, a lesion of the pancreas can by no means be excluded on the ground that the stools contain no excess of fatty substances.

*Creatorrhea.* When, in addition to impaired splitting or utilization of fats, there is obvious failure to digest protein, Garrod believes the evidence of a pancreatic lesion is well-nigh conclusive. The simplest test of creatorrhea is the recognition of striped muscle fibers in the stool. The test is not affected by blocking of the bile duct. Excessive excretion of nitrogen in the stools and a consequent inordinate loss of nitrogen as determined by metabolic studies, but azotorrhea is far less distinctive than the escape of striped muscle and nuclei.

*Tryptic Digestion.* Tests for tryptic digestion fall into three main groups: (1) Some of them aim at recovering duodenal contents, (2) some rely on the action of pancreatic juice on so-called messengers sent along the intestinal tract, and (3) others, upon the estimation of the tryptic action of the feces. (1) Of the first named, the duodenal tube is the means of obtaining duodenal juice direct, the tryptic power of which is then determined. (2) The messenger tests include Sahli's test of a formalin hardened capsule containing a drug easily detected in the urine or saliva, the idea being that the capsule is attacked only by tryptic activity. Included also under this heading are Schmidt's beef cube test and Kashiwado's test in which stained nuclei from the calf's thymus are ingested. Recovery of such material from the bulky feces of a pancreatic patient is a task of no mean dimensions. (3) Of methods which test the tryptic power of feces, that of Gross is often used. It is based upon the digestion of casein by an alkaline extract of the feces. Failure to digest casein offers strong evidence of pancreatic inefficiency, but seeing that other ferments in the feces can act like trypsin, a positive outcome of the test, unless very pronounced, has less value.

*Carbohydrate Digestion.* Wohlgemuth's tests of diminished output of diastase in the stools and an increase in the blood and urine, are common phenomena in cases of lesions of the pancreas, and Garrod believes the test is one of the best and most easily and rapidly carried out. It, however, shares the uncertainty which pertains to pancreatic tests in general, and although a conspicuous excess of diastase in the urine is strongly suggestive of disease of the pancreas, a normal excretion in no way excludes disease of the gland. A great objection to the test is that in renal disease the power of the kidney to eliminate is so seriously impaired that the estimation of diastase in the urine is utilized as a test of renal efficiency and this is enough to deprive the test of dependability and individuality. Garrod prefers the diastase test to Loewi's test.



*Evidence of Failure of Internal Secretion of the Pancreas.* The presence of sugar is of itself insufficient evidence of pancreatic disease, and absence of glycosuria affords no argument against the presence of disease of this gland. Sugar tolerance tests are very useful. Cammidge's reaction is undoubtedly concerned with pancreatic derangements and when observed, supplies a contribution to the building up of a diagnosis. It fails many times in cases of severe disease of the gland. "The test has suffered from the fact that too much has been expected from it, and perhaps that too much has been claimed for it, and because it has not proved so decisive as was hoped, its utility has not received the credit which it deserves."

Garrod presents in great detail 4 cases illustrating the protean phenomena in pancreatic disease and concludes his brilliant article by saying:

"It will be evident, from all that has gone before, that practically every sign, symptom or test may fail at times, and that in each individual case we need to balance the quantity and quality of the evidence for and against lesions of the pancreas. In a word, we come back to Wardell's statement of 1871. It is still true that 'no symptoms are pathognomonic of pancreatic disease. An assemblage of symptoms points to the probability of its lesion.' But we have at our disposal a far greater assemblage of symptoms than Wardell had, and in not a few cases the degree of probability is not to be distinguished from certainty.

"That is as much as can be expected when we are dealing with a problem, the solution of which rests so largely upon circumstantial, rather than direct, evidence. If we cannot claim for the diagnosis of pancreatic disease the clear-cut, direct answers obtained in some other regions of clinical medicine and surgery, we may none the less regard with complacency what has, so far, been accomplished in this field, by the application of physiologic discovery at the bedside, by the coöperation of the laboratory and the ward."

Labbé<sup>86</sup> has made a special study of the nuclear digestion in 111 cases representing various pathologic conditions of the digestive tract. The value of the test depends upon the rapidity with which the cubes of meat travel through the bowel. The optimum time is twenty to twenty-six hours; if it is longer, microorganisms can digest the meat, and, if shorter, there is not enough time for the pancreatic ferments to act.

In diabetics the results are not uniform. Of 19 cases without emaciation, 12 showed complete digestion and 7 incomplete. Of 26 cases of diabetes with emaciation there were 12 with complete digestion, 6 with imperfect digestion, and 1 in which there was no evidence of digestion.

In 4 cases of cancer of the head of the pancreas, digestion was always distributed, and Labbé regards it as an important diagnostic sign.

In 6 cases of catarrhal jaundice, 2 had complete and 4 incomplete digestion, showing some participation on the part of the pancreas in this condition.

In 11 cases of cirrhosis of the liver, 4 had complete, 4 incomplete, and 3 no digestion of the meat cube.

<sup>86</sup> Bull. de la Soc. méd. de hôp., 1920, xxvi, 784.



Of 7 cases of cholelithiasis, 5 had complete and 2 absence of digestion, a fact which is in accord with surgical teaching, that there is often an inflammatory sclerosis of the head of the pancreas in gall-stone.

Eight cases of chronic enteritis, 1 complete, 4 incomplete, and 3 no digestion, evidencing some involvement of the pancreas.

Two cases of gastric aepsia had incomplete or absent digestion.

Labbé warns that an absolute diagnosis must not be made on this test alone, but he is convinced of its dependability and great value taken in conjunction with physical and laboratory findings.

### DISEASES OF THE PERITONEUM.

**Acute Diffuse Peritonitis.** The article by Hughes,<sup>87</sup> although based on war experience with gun-shot wounds of the peritoneum, has many suggestions which may be made use of in civilian practice when peritonitis from disease occurs.

Early symptoms are due to Nature's method of dealing with the disease as soon as infection has healed the peritoneal cavity, a splint is applied in the form of a rigid abdominal muscle. There is pain and tenderness coinciding with the hyperemia of the peritoneum and later there is a definite palpable mass, due to adhesions, adherent omentum and the diseased part of the gut. With progression of the disease, the tenderness becomes more general the whole abdominal wall is rigid, distention sets in, and vomiting commences. Constipation is absolute, there is not passage of flatus, vomiting increases in frequency, the patient rapidly becomes dehydrated, there is hiccough and a typical abdominal facies, the tongue is dry and coated, sordes appear on the lips and teeth, vomiting later becomes coffee-ground, the pulse becomes more rapid, and thready and finally the patient dies of toxemia. Vomiting of the coffee-ground variety is of very serious import and denotes a very severe toxemia.

*Treatment.* Many authorities have advised treatment on the following lines:

1. Removal of the cause at the earliest possible moment.
2. Drainage of the peritoneal cavity after performing lavage or no.
3. Abolition of the distention by means of graduated doses of calomel, subcutaneous injections of pituitrin or eserin, turpentine enemata, artificially emptying the distended bowel and the like.
4. Control, if possible, of the vomiting by various drugs or gastric lavage.
5. Saline, either subcutaneously or rectally, and stimulants.
6. Suitable nourishment.

On (1) all are agreed.

2. Can this peritoneal cavity be drained. and, if so, what is drained away? Postmortem examinations have shown that a drainage tube is walled off by adhesions like any foreign body within a few hours of insertion. "The degree in which adhesions are thrown out is a very

<sup>87</sup> British Medical Journal, September 20, 1919, p. 873.

important measure of the degree of the patient's vitality." Hughes properly questions that if protective adhesions are being thrown out, what are we trying to drain away? and he answers. "a protective fluid of first rate vitality." If a case of general peritonitis can receive help early, it suffices to mop out carefully any obvious pouches in the region of the area of operation with dry sterile swabs and avoid drainage. Purulent peritonitis demands drainage but this type is hopeless from the first. If lymph is present it should be left undisturbed, and it is unwise to attempt to unravel any coils of intestines which are matted together, for this matting reduces the area of absorption to a minimum. Peritoneal lavage does no good for it spreads infection and also washes away a highly valuable fluid.

3. What is the significance of a distended intestine? The gut is acutely inflamed, its musculature is rendered incompetent partly as a result of toxemia and inflammation and partly as a result of abnormal gas formation. "Would we suggest to a patient who was suffering with acute cellulitis of both legs, that he should get up and run about in order to effect a cure?" Any treatment directed toward reducing distention tends to increase peristalsis and hence infection is spread. Rest is the only rational treatment and this is best secured by morphin grains one quarter every eight hours, and atropin gr.  $\frac{1}{100}$  every twelve hours. Constriction of the pupil calls for reduction to grains one-quarter every twelve hours, and this occurs usually at the end of forty-eight hours. These drugs are continued until vomiting ceases and flatus is passed and this is seen at the end of the fourth or fifth day.

4. Vomiting is a means of eliminating the toxin, and why devise means for checking it? Biliary vomit which gradually becomes clearer is of good omen; coffee ground vomit is serious, but if it changes to biliary vomit the prognosis is good. If, on the other hand, the vomit becomes fecal, there is intestinal obstruction and further operation is indicated. In 2 of Hughes's 21 cases, this occurred, and both recovered, and in both instances there was obstruction at the ileocecal junction. Vomiting, then, should be encouraged.

5. But the dehydration resulting from continuous vomiting, calls for replacements of fluid, nine to ten pints of saline in twenty-four hours. Swelling of the feet or water-logging of the lungs must be guarded against. At the end of forty-eight hours, the patient needs less fluid and it may be reduced to five pints. Copious drinks of water with sodium bicarbonate and sodium citrate are given by mouth. As soon as the vomiting has ceased, administration of saline is withheld, and since the inflammatory condition is now subsiding, on no account should purgatives be given. Flatus is now passed and generally an offensive liquid stool. Bismuth and compound tincture of camphor can be given with benefit as soon as the vomiting has ceased.

6. For the first forty-eight hours no nourishment is required, saline being all that is necessary. On the third and fourth day, glucose is given by the rectum. As soon as the vomiting has ceased, albumen water and glucose may be given, frequently, but in small amounts. Water may be administered freely. At the end of a week, milk and

soda water, raw eggs, and a little custard may be given, and from this date, the diet may be gradually increased. On the tenth or twelfth day, castor oil may be prescribed and from this date all anxiety is usually at an end.

In Hughes's 21 cases, the cause of the peritonitis was:

Appendicular abscess . . . . .	6
Perforated gastric ulcer . . . . .	1
Trauma . . . . .	8
Intestinal obstruction with gangrene . . . . .	3
Intestinal obstruction with perforation of the bowel . . . . .	1
Pneumococcal . . . . .	2
	<hr/>
	21

There was only one death—a case of intestinal obstruction with gangrene of the gut.





# DISEASES OF THE KIDNEY.

BY HENRY RAWLE GEYELIN, M.D.

**Nephritis.** In reviewing the literature on nephritis for the past year and contrasting it with that of other years, one is struck with the great scarcity both of clinical and experimental investigation. This is undoubtedly due, at least in part, to the fact that the suspension of investigative work in most clinics during the war has just begun to make itself felt.

It is also noticeable that, with a few exceptions, such work as has been done is not fundamental in character and there has been a great deal written based on observations of clinical material where satisfactory methods of control have been lacking and where conclusions based upon insufficient evidence, have been advanced. For these reasons no attempt is made to review or comment on all the published work of the past year, but rather to confine the present article to the more important experimental and clinical observations and a critical discussion of their bearing upon the various etiologic, functional and therapeutic problems of renal disease.

THE STUDY OF KIDNEY FUNCTION in chronic renal disease by means of the so-called "functional tests" which include the various dye tests, estimation of non-protein nitrogen content of the blood (urea, uric acid and creatinin), the various formulæ for the measurement of the rate of urea excretion, the measurement of the sodium chloride and water exchange and the "dietary test days," of which the Mosenthal test day is the most popular in this country, has given us certain valuable information in the treatment of our patients and has, when correlated with the clinical symptoms, greatly added to our prognostic ability. The functional tests, although they have added much to our knowledge of the manner in which the normal function of the kidney is accomplished, have not definitely settled this question, nor have they, even with the help of careful consideration of clinical findings, enabled us to predict the anatomical lesion in various forms of acute and chronic nephritis.

It may be noted here that some observers—chief among them Volhard and Farr<sup>1</sup>—have attempted to classify renal disease upon a functional basis, and correlate the anatomical lesions found at autopsy with the functional findings during life. This has proved little, if any, more satisfactory from a diagnostic standpoint, than did the older anatomical method of classification, so that we are forced to the conclusion that any classification of renal disease whether it be upon a functional basis, a symptomatic basis or upon an anatomical basis, has so many limitations

<sup>1</sup> Die Brightsche Nierenkrankheiten, Springer, Berlin, 1914.

and exceptions that it is inexact from a scientific and confusing from a therapeutic point of view. Any attempt to correlate all these methods of classification each with the other is equally disappointing and tends to further confuse an already complicated subject. "Chronic interstitial nephritis," "chronic hypertensive nephritis," "chronic parenchymatous nephritis," or "nitrogen retention nephritis" may serve as terms expressive of our desire to differentiate various forms of nephritis, upon a functional, symptomatic or an anatomic basis. Clinically, such entities are rarely clear-cut or well-defined and even when they are definite as clinical pictures, experience has taught us that they certainly cannot always be correlated with their corresponding pathologic entities in pure form at autopsy.

To illustrate—it does not serve any useful purpose to speak of the "nitrogen retention" type of nephritis, if by that term we wish to convey a definite pathologic picture, because in the nitrogen retention type of chronic renal disease, the symptomatic and functional pictures are variable and the anatomic lesions may be combinations of the many pure types of renal lesions. On the other hand, even as at autopsy, it is uncommon to find pure glomerular or pure tubular nephropathies, so also is it all the more difficult to isolate their clinical or functional analogues, such as pure hypertensive nephritis, pure salt retention nephritis, etc., or any pure form as such, and then try to associate the symptomatic or functional with the anatomic forms. Particularly is this true with our lack of definite knowledge of what the symptomatic or functional response is to pure anatomic forms of nephritis. Obviously the difficulty is greater in determining what the symptomatic or functional response is in the mixed anatomic forms of kidney disease.

Atchley,<sup>2</sup> in an article reviewed by Christian, *PROGRESSIVE MEDICINE*, 1919, discusses the result of a study of 8 cases of acute nephritis, and offers an excellent summary of what seems to him to be the most rational point of view with which to approach the whole subject of the classification of nephritis. Most observers will doubtless agree that Atchley's conclusions regarding classification, although they are only intended to apply to cases of acute nephritis are equally applicable to cases of chronic nephritis. I have, therefore, taken the liberty of changing parts of the following quotation so as to make Atchley's views on classification apply to all types of nephritis: "In treating diabetes we are satisfied, clinically, with its simple terminology and proceed to investigate the peculiarities of the disease in a particular individual. In like manner it would seem logical in nephritis to speak of 'acute' or 'chronic' renal syndromes and investigate the variations in 'clinical,' 'functional' and 'anatomic findings,' in each case without demanding that every variation be added to the terminology of the diagnosis."

The concluding paragraph in Atchley's article is as follows: "One must express the feeling that the investigation of this disease (nephritis) has been hindered by an interest too closely restricted to the kidneys. A broader study of the chemical balances of the body as a whole may

<sup>2</sup> *Archives of Internal Medicine*, 1918, xxii, 370.



demonstrate that the kidney is of secondary importance," both from an etiologic and pathologic standpoint.

Although this is a suggestion that has been offered in the past by some observers it has not met with the degree of consideration and investigation that it deserves. It seems to me that this is a very important field of research and one that demands urgent consideration. One of the reasons that so little investigative work has been directed along the lines that Atchley suggests, has been our lack of facilities and convenient technical methods; now that the latter are supplied to us by the recent elaboration of methods in microchemistry and the rapid advances in physical chemistry, it is probable that fundamental additions to our knowledge of renal disease will soon be made. The study of the etiology and the nature of edema offers a particularly appropriate subject for the application of physical and chemical methods and should lead to findings of fundamental importance.

*Experimental.* During the past year, MacNider,<sup>3</sup> working on dogs, has made an important contribution to our knowledge of the relationship between kidney function and definite renal lesions. After many years of experimenting with uranium in the production of nephritis, he has been able to produce with constancy, definite renal lesions under certain well-established experimental conditions. These lesions are in the first stages those of an almost pure tubular nephritis. After a period of several days, depending on the age of the animal, the acute lesions produced in the tubules either cause death, as in some of the old dogs, or as in the younger dogs, go on to a stage of repair with the subsequent production of a mixed tubular and glomerular nephritis with some interstitial involvement. MacNider, therefore eventually, reproduces a mild grade of chronic nephritis, anatomically comparable to certain forms of renal disease in man and differing only in that it apparently is not progressive.

In conjunction with the histologic observations made upon the kidneys after sacrificing the animals at various stages of the nephritis, the author has carefully studied the functional activity of the kidney at each stage in the progress of the disease, using for this purpose the phthalein test and the urea and creatinin concentrations of the blood. He has also studied the disturbances in acid to base equilibrium produced by uranium nephritis, using the Marriot method of plasma hydrogen ion concentration as an index of acid-base disturbance. Finally, MacNider has observed the effect of this type of experimental nephritis upon the total output of urine and upon the production of albumin and casts. No observations upon blood-pressure were made. A summary of his results is best given in the following conclusion quoted from his article:

"1. The acute tubular nephropathy which is produced by uranium is associated with the ability of the metal to effect a disturbance in the acid-base equilibrium of the blood. The tubular injury is more marked in an old animal than in a young animal. In an old animal the depletion

<sup>3</sup> Archives of Internal Medicine, 1920, No. 1, xxvi, 1.

of the alkali reserve of the blood occurs more rapidly and is more pronounced than is the case in a young animal.

2. This injury to the kidney is indicated functionally, first by a reduction in the elimination of phenolsulphonephthalein and later by a retention of blood urea and creatinin.

3. Associated with the establishment of such injury both albumin and casts appear in the urine. The amount of albumin in the urine is no index of the severity of the pathology in the kidney or the degree of functional disturbance. The quantitative output of albumin may show a progressive decrease, while at the same time the elimination of phenolsulphonephthalein is rapidly decreasing, and both urea and creatinin are showing a retention.

4. A certain number of the animals rendered acutely nephropathic by uranium have recovered from the acute injury with the development of a chronic nephropathy. Those animals which effected a recovery were young animals. The old animals were unable to establish and further these changes of repair which lead to recovery with a chronic nephropathy. The changes in the kidney during the period of recovery have consisted in the regeneration of tubular epithelium of a flattened and less specialized type and of the production of chronic obliterative and sclerotic changes in the glomeruli. With the establishment of this type of chronic injury there occurs an increase in the alkali reserve of the blood which may reach the point of normality. There is an increase in the elimination of phenolsulphonephthalein and a decrease in the retention of blood urea and creatinin.

5. From these anatomic and functional observations the inference is drawn that the tubular epithelium is of more importance in maintaining a normal acid-base equilibrium of the blood, and is more concerned with the elimination of phenolsulphonephthalein urea and creatinin than is the vascular mechanism of the kidney.

6. Similar observations have been made in a group of naturally nephropathic animals in which the chronic injury to the kidneys has consisted in a glomerulonephropathy with histologically well preserved tubular epithelium. In such animals the reserve alkali of the blood may be normal, the elimination of phenolsulphonephthalein may be only slightly reduced, and there may be no retention of blood urea and creatinin. When, however, an acute tubular injury is superimposed on this chronic injury by uranium or mercuric chloride there occurs an early edema and necrosis of the tubular epithelium without the development of an acute injury to the glomeruli. Such an injury has been associated with a rapid depletion of the alkali reserve of the blood and an associated decrease in the tension of carbon dioxide in the alveolar air. The acute injury is expressed functionally by a rapid reduction in the elimination of phenolsulphonephthalein and by a retention of blood urea and creatinin. The animals become acutely anuric and die in convulsions or in a coma which may not be preceded by convulsions.

7. The present investigation which has been concerned with certain functional and anatomic studies in different types of nephropathic processes, tends to minimize the importance of the glomeruli as a func-



tional unit and to emphasize the relative importance of the tubular epithelium. The investigation furthermore points out the influence of a disturbance in the acid-base equilibrium of the blood on the histology and functional capacity of the renal epithelium."

Arterial lesions, and the actual injury to the glomerular units of the kidney, according to MacNider, played no part in the loss of the kidney's power to excrete urea, creatinin and phthalein, but the injury to the tubular units had a definite effect upon the power of the kidney to excrete these test substances. MacNider was apparently not concerned with the manner in which these functional changes were brought about, *i. e.*, whether by increased reabsorptive power of the tubules or by loss of their secretory activities, the latter being contrary to Cushney's conception of the function of the tubules. MacNider merely offers the definite association of tubular lesions with marked loss of certain functional capacity and the partial or complete recovery of this functional capacity associated with varying degree of subsequent regeneration of the tubular epithelium and the development of a chronic glomerular nephropathy. There is no question, however, as to the inference drawn, namely; that the tubules in contrast to the glomeruli play the most important part in determining the mode of secretion of urea, creatinin and phthalein because tubular disease in almost pure form renders the kidney maximally insufficient as far as the elimination of these test substances is concerned, whereas the milder chronic, vascular and interstitial type of nephritis that follows tubular regeneration, only slightly, if at all, lowers the kidney's ability to excrete these test substances. Until some satisfactory form of experimental nephritis, in which extensive vascular changes in pure form can be produced and these correlated at various stages, with functional findings, we will not know to what extent secretory function, as estimated by functional tests, is affected in the pure vascular type of nephritis.

It is possible that the studies of MacNider on tubular nephritis, if extended to include their effect upon the excretion of salt, water, uric acid, and phosphates together with blood-pressure determinations might, in association with similar studies upon pure glomerular nephritis, throw further light upon the normal secretory function of the kidney and the exact manner in which this function is perverted. Work among these lines in the past has been inconclusive either because of incompleteness of functional studies or because of failure to produce uniform kidney lesions in pure anatomic form, or both.

Cushney's<sup>4</sup> theories on normal kidney function, *i. e.*, glomerular filtration plus tubular reabsorption denying a secretory function of the tubules have been pretty generally accepted, yet there is no adequate experimental evidence to establish this theory as a fact. It is possible that experiments as indicated would furnish evidence as to whether the tubules are concerned in the secretion of the above mentioned test substances, or are merely reabsorptive units for these various components of the glomerular filtrate.

<sup>4</sup> The Secretion of Urine, Longmans, Green & Co.



For many years clinicians have recognized the beneficial effect of restricting protein food in the treatment of certain types of nephritis and in more recent years it has been possible to demonstrate that protein restriction will greatly decrease the non-protein nitrogen of the blood when a retention of these products has occurred. Partly as the result of these observations, the attention of many investigators has been directed toward the possibility that nephritis may be produced by long-continued use of diets high in protein. Actual demonstration of this assumption has always been wanting.

During the past year, Newburgh,<sup>5</sup> in a series of experiments on rabbits, claims to be able to produce definite renal lesions in these animals comparable to certain definite anatomic forms of nephritis as seen in man. The manner in which these are produced is by feeding diets which contain amounts of pure protein greatly in excess of the normal metabolic requirements of the rabbit. He has chosen to employ egg whites, casein and soy bean protein in these experiments. All these substances produce albuminuria and casts, when fed in quantities, two to three times in excess of the normal protein requirements.

Description of the anatomic lesions in the kidney of the animals fed on egg whites are lacking in detail but the author summarizes the results of these experiments by saying:

"First: When rabbits eat several egg whites daily evidence of a renal injury is very quickly and constantly noted.

Second: When rabbits absorb the digestion products of egg white in sufficient quantity for a considerable time, a well marked acute or sub-acute nephritis may result."

The time required to produce nephritis in these animals varies from three and a half to seven months.

With the rabbits fed on casein we note that a moderate to severe type of nephritis is produced, albumin and casts being constantly present. The kidneys on microscopic examination showed very marked edema and engorgement. There were numerous red cells scattered through the subcapsular spaces and the lumina of the tubules. Very many casts were seen. The other organs were normal. The type of renal disturbance found strongly suggests that the symptoms had been caused by acute nephritis. He found that when fifteen grams of casein had been fed daily that there was no injury to the kidneys, but that when the intake of casein was increased to thirty grams, there was a well marked "deleterious effect" on the kidney.

With the rabbits fed on soy bean more definite protocols are given and a more definite type of nephritis is produced with greater constancy. These animals also showed definite urea retention of marked degree. The type of nephritis produced was what is described by the pathologist as the "secondarily contracted kidney."

Incidentally, Newburgh<sup>6</sup> has observed that a certain degree of arteriosclerosis of the aorta, particularly well marked in the first portions of the aorta, is found in rabbits after high protein feeding.

<sup>5</sup> Archives of Internal Medicine, 1919, No. 4, xxiv, 359.

<sup>6</sup> Squier, Theodore L.: Archives of Internal Medicine, 1920, No. 1, xxvi, 38.

These results are very interesting and are a valuable contribution to our knowledge of experimental nephritis, but it is extremely doubtful whether there is any analogy between the production of this experimental form of nephritis in rabbits and the possibility that certain similar forms of human nephritis may be produced by overeating of protein food. In fact, no such conclusion would be justifiable on the basis of the experiments cited. (The author does not attempt to draw any.) In the first place, rabbits normally secrete a urine that is alkaline and over-feeding with soy bean protein produces an acid urine. Newburgh controlled the possibility that this change in urinary reaction was the cause of the nephritis by feeding sodium bicarbonate and maintaining an alkaline urine during the whole course of the experimental period and was still able to produce nephritis. A second consideration is that it is doubtful whether the human gastro-intestinal system would tolerate such an excess of protein as Newburgh was able to feed his rabbits over a period of time long enough to produce nephritis. Thirdly, it seems that the rabbit is peculiarly adaptable for such experiments because of the ease with which it is possible to produce evidence of marked arteriosclerosis. A fourth consideration which renders highly improbable any analogy between these experiments and the possibility of producing nephritis by such means in man, is that the rabbit is essentially herbivorous and would be more apt to react pathologically to such a marked perversion of its normal metabolism than would man, who is of the omnivorous type and in whom an increase in the protein intake of a degree comparable to that administered by Newburgh, while it would be a perversion of the normal diet, would be one of lesser degree.

RENAL FUNCTION. Meyers<sup>7</sup> reviews the more recent literature on the subject of urea, uric acid and creatinin content of the blood in nephritis and summarizes his own series of observations made over a period of years. He again emphasizes the importance of blood uric acid determination as an index of early nephritis, calling attention to the fact that the kidney possesses the power of concentrating uric acid only twenty times, whereas it has the power to concentrate urea eighty times and creatinin one hundred times, therefore that substance (uric acid) which is excreted with the greatest difficulty is the first one to undergo retention when the kidney is diseased. Meyers as well as Bauman, Hansman, Davis and Stevens,<sup>8</sup> regards an increased uric acid concentration in the blood (when gout is excluded) as the most delicate test for renal function at our disposal. Benedict<sup>9</sup> believes blood uric acid above 3 mg. per 100 c.c. to be definitely abnormal and to be suggestive of kidney involvement even when other symptoms of such a condition may not have appeared. He says that in 150 blood uric acid determinations on normal individuals he has seldom observed instances in which the uric acid of the blood exceeded 3 mg. per 100 c.c., that he believes that when figures of over 3 mg. do occur, even in the absence of any other

<sup>7</sup> *Journal of Laboratory and Clinical Medicine*, 1920, No. 6, v, p. 343; No. 7, p. 418; No. 8, p. 490.

<sup>8</sup> *Archives of Internal Medicine*, 1919, No. 1, xxiv, 70.

<sup>9</sup> Personal communication.



signs of nephritis, that this is indicative of a disturbance of elimination or metabolism which may, in the natural course of events, terminate in gout or nephritis.

Bauman, et al., give 2.5 mg. per 100 c.c. of blood as the upper limit of normal, while Meyers believes that 3 mg. is the upper normal limit.

While the view that blood uric acid above 3 mg. is indicative of early renal disease or gout in an otherwise normal individual may be correct, proof of this assertion can only be obtained by long-continued observation on patients who subsequently develop either gout or nephritis, these patients having had throughout the period of investigation a high uric acid content of the blood.

Upham and Higley<sup>10</sup> agree with Myers and Benedict in accepting 3 mg. per 100 c.c. of blood as the high normal limit. They also present series of cases composed of non-nephritics, doubtful nephritics and true nephritics, in which they lay much stress upon the functional value of determining the kidney's ability to concentrate uric acid, employing as their index of ability to concentrate the ratio  $\frac{\text{mg. blood uric acid}}{\text{mg. urine uric acid}}$  (the urine being collected three or four hours after a uniform breakfast and at the time of taking the blood). It is interesting to observe that the authors' protocols show blood uric acid of 4 mg. per 100 c.c. or over in four of the patients in the non-nephritic group whose index of concentration is within normal limits. Thus, Upham, and Higley claim that the ratio of excretion of uric acid is a more valuable guide to the functional capacity of the kidney than is the blood uric acid alone. The group of cases which are clinically non-nephritic show a concentrating ability (as determined by the above index) of 20 or over. The doubtful nephritics show a concentrating ability of 18.4 or below while the true nephritics have a concentrating power of 14 or below.

In the group of ten "questionable cases of nephritis" there are three patients who have a blood uric acid which is well within normal limits and yet their indices of concentration, 14, or below would put them in the same category with the proved nephritics. These three patients also showed albumin, two of them with casts. Upham and Higley believe that the patients in this group belong with the positive nephritics "and that such belief will be verified by the further clinical observations of these cases. Such observations are now under way, together with the study of other cases both from a clinical and concentration standpoint."

This same principle of determining the ability of the kidney to concentrate non-protein nitrogenous constituents of the blood has been employed by Addis<sup>11</sup> and Watanabe<sup>12</sup> in the case of urea and it has the merit of simplicity when compared with the more complicated formulæ of Ambard or McLean's modification of it. But as Addis and Watanabe have shown, the ratio between the urea concentration in the urine and that of the blood, where the urine is collected for short periods during the day, may vary widely and such variations are not explainable by any

<sup>10</sup> Archives of Internal Medicine, 1919, No. 5, xxiv, 557.

<sup>11</sup> Journal of Urology, 1917, i, 263.

<sup>12</sup> American Journal of the Medical Sciences, 1917, cliv, 76.



known cause. McLean, of course, tried to diminish this variation by taking the fourth root of the most variable factor, but this method of measuring the rate of urea excretion has not yielded information regarding the functional capacity of the kidney of as much clinical value as many other of our functional tests. During the past year, Austin, Stillman and Van Slyke<sup>13</sup> have presented a formula for measuring the rate of urea excretion; this formula being based upon a modification of the McLean index. These authors have observed a constant relationship between the ratio of urea excretion to blood urea concentration when other factors (chiefly the volume of urine) are taken into consideration. A summary of their findings is best expressed in the following quotation:

"On the basis of our own observations on normal human subjects, and of those of McLean and Addis, we find that the ratio of urea excretion to blood urea concentration varies considerably in the normal subject. These variations cannot be explained by variations in the concentration of urea in the urine. A constant relation has, however, been observed between these variations and changes in the rate of urine volume output.

The relationship that holds may be thus expressed:

$$\frac{D}{W} = KB \frac{V}{W}$$

D, grams of urea excreted per diem, calculated from a seventy-two-minute period.

B, grams of urea per liter of blood.

V, liters of urine excreted per diem calculated from a seventy-two-minute period.

W, Body weight in kilograms.

In all observations on normal human subjects as published in the data of McLean and Addis and in our own observations, the value of K is  $7.5 \pm 3$ .

The influence of increasing the rate of urine volume output on the rate of urea excretion holds, however, for all normal subjects studied only up to a certain limit, which we call the 'augmentation limit,' which appears to be characteristic for the individual, and which has in our experience been between the rates of 3 and 5 liters per diem. Beyond this 'augmentation limit,' the limit is to be used as V in the formula in place of the urine volume output observed."

It is hoped that the application of this method of measuring the rate of urea excretion will be extended to include a large group of widely divergent types of nephritis, and that the results will demonstrate that the physiologic laws governing the rate of excretion of urea are capable of mathematical expression. It is also hoped that the results of such a study will furnish us with a more delicate and mathematically comparative index of the degrees of renal damage than have any of the functional tests now at our disposal.

<sup>13</sup> American Society for Clinical Investigation, Journal of the American Medical Association, June 5-26, 1920, vol. lxxiv.

There is great need of such a functional test, particularly in that large group of mild or early nephritics, where some slight impairment of the urea function probably exists, but which cannot be detected by Ambard's or McLean's index, nor by the quantitative estimation of urea in the blood alone. Until further attempts can be made to prove the clinical value of this new index all that can be said at the present time is that as a measure of kidney function in nephritis the estimations of uric acid, creatinin and urea in the blood and their interpretation, when taken in connection with other findings, are of more clinical value as guides to impairment of function and prognosis in renal disease than any of the various indices expressive of excretory rate.

Mosenthal's<sup>14</sup> "Nephritic Test Day" (dietary) may under certain conditions of interpretation be very useful as a measure of functional capacity of the kidney in nephritis. The variations from the so-called normal which have seemed to me of most value in interpreting functional impairment with this test are the following:

1. Fixation of specific gravity at a low level—(fixation at a high level is of doubtful significance and may be found in individuals who show no other evidence of nephritis).

2. Marked deficiency in ability to concentrate salt and nitrogen (here again, slight deficiency is of little, if any, clinical significance).

3. Marked increase of the night urine.

When such variations as the above, either alone or combined exist other functional tests such as blood urea, phthalein or the total salt and fluid exchange are usually so definitely impaired that the further information given by the "Dietary Test" is only confirmatory and scarcely warrants the time and attention to detail which the test requires. Many observers do not agree, that the slight variations in specific gravity or slight variations from the normal in the other factors involved in the test, are of the same diagnostic value in cases of suspected nephritis as is claimed by Mosenthal.

If, among the non-protein nitrogen constituents of the blood (uric acid, urea and creatinin), we regard retention of uric acid as the most delicate and earliest evidence of functional impairment, we should then always find high figures for uric acid when the functional impairment of the kidney has advanced to a stage where the urea is being retained, such is usually the case, but I have observed in 2 cases of nephritis a high figure for blood urea (50 to 70 mg. urea) when the blood uric acid was below 3 mg. per 100 c.c. This is a very uncommon finding but emphasizes the importance of determining both uric acid and urea in any suspected case of nephritis. I cannot recall, however, ever having seen a retention of creatinin without a high blood uric acid and a high urea content of the blood.

Denis and Minot<sup>15</sup> find that the inorganic phosphates in serum in a large series of "pathologic condition" other than nephritis or cardiorenal disease may vary from 1.2 to 3.1 mg. of phosphorus per 100 c.c. of plasma. Blood<sup>16</sup> gives results on normal persons which range from 1.8

<sup>14</sup> Archives of Internal Medicine, 1915, xvi, 733.

<sup>15</sup> Ibid., 1920, No. 1, xxvi, 99.

<sup>16</sup> Journal of Biological Chemistry, 1918, xxxvi, 49.

to 4.3. The authors have also studied a group of cardiorenal and nephritic cases and they conclude that 65 per cent. of these cases taken at random from material in the hospital wards, give unmistakable evidence of phosphate retention. The figures range from 4 to 28 mg. per 100 c.c. of blood. "Fatal cases showed a rapid and progressive increase in plasma phosphate, increases of more than ten times the maximum normal value having been noted; the non-fatal cases, even though the patient was seriously ill, presented a relatively slight increase."

The authors suggest the possible prognostic importance of the determination of the inorganic phosphates in nephritis.

The phosphate retention was often not present when the blood urea was high and the phthalein low. Such cases usually improved—at least, were able to leave the hospital. It would seem that phosphate retention like creatinin retention was a late manifestation in renal disease, and may furnish equally valuable prognostic information. There was no definite relation observed between the plasma phosphate and the alkaline reserve of the blood.

In reviewing a considerable number and variety of functional tests as performed on a large number of nephritic patients in the wards of the Presbyterian Hospital during the past six years, the following, in a general way expresses the conclusions arrived at: The retention of blood uric acid reveals the earliest evidence of the kidney's inability to excrete the non-nitrogenous substances of the blood. Of itself and unsupported by any other evidence, high uric acid in the blood is not diagnostic of nephritis.

Next in order of delicacy as a functional test is the retention of blood urea which is a much more valuable test both from a clinical and diagnostic standpoint. Retention of urea always indicates definite impairment of the kidney's ability to excrete the non-nitrogenous elements of the blood. This lack of ability to excrete urea may be overcome by lowering the protein intake. The creatinin concentration of the blood yields the most definite information regarding prognosis. When there is retention of creatinin it can be stated that the outlook for duration of life is very limited. The phthalein test is also a valuable method of measuring the kidney function from a diagnostic standpoint and in the absence of edema, definite evidence of kidney insufficiency is indicated by an excretion below 40 per cent. in two hours. This insufficiency may be temporary, as in cardiac decompensation. Many observers believe that 50 per cent. is the upper limit of normal, but patients have been observed in whom no other evidences of renal disease or genito-urinary tract obstruction can be found except a phthalein excretion of between 40 to 50 per cent. The determination of the total twenty-four-hour salt and fluid exchange together with the determination of the salt concentration, the total amount of urine and the specific gravity in day and night urine, is of great diagnostic and therapeutic value in that type of nephritis where impaired salt and water function of the kidney is involved. In this type of nephritis, it is impossible to emphasize too strongly the importance of continued observations of body weight.



Many other tests of function such as McLean's Index, Mosenthal's Test Day, Plasma Chloride Concentration, Sodium Chloride Index, etc., have been routinely employed for varying periods of time but have not proved of sufficient diagnostic or prognostic value to warrant continuation of their use except in rare instances.

**ETIOLOGY OF NEPHRITIS.** The past year has yielded no new theories regarding the etiology of nephritis but there is still a tendency on the part of some investigators to lean toward the theory of the infectious origin of nephritis, at least, in a certain limited group of nephropathies.

The extreme view that a focus of infection is the etiologic factor in all cases of nephritis is certainly losing popularity. This is due to the lack of confirmatory evidence both clinical and experimental. Even when we suspect a focus of infection as an etiologic factor in the production of nephritis it is only seldom that we are able to prove it either during life or at autopsy, and furthermore, even when a focus of infection is recognized very early, we are rarely able to arrest the course of the disease by eliminating this focus. Christian<sup>17</sup> expresses what may be considered as the prevailing views on this subject, as follows:

"Of its (nephritis) etiology we know surprisingly little in any exact sense, though the view is receiving increasing support that many of the cases have their primal cause in an infection of bacterial nature, more frequently of the streptococcus group. Even granted, however, that organisms of the streptococcus group originate the renal disturbance, we are not helped much in the matter of treatment, because, in case of the known non-renal streptococcus lesions, we are able to treat only by elimination or drainage of a focus of infection, and can do little, if anything, toward counteracting the toxic substances that are produced and distributed to the body organs. If actually resulting from an infection, the chronic renal lesion presents itself months or years afterward, too late to be helped much by removal of the focus of infection even if still present. In other words, in the earlier, easily treated stages of the infection, the infection may pass unrecognized; or, what happens more frequently, there is nothing to indicate the beginning of a lesion in the kidney which slowly and gradually will develop into a recognizable nephritis. In the later stages when the renal lesion is easily recognized, the focus is no longer existent, or is present, its removal can change but little the renal damage already done. I have been very much struck in my own experience, with the relatively few cases of chronic nephritis that seem to have been a direct sequence to a demonstrated infection or infectious disease; most of these have belonged to a rather distinctive group of cases, progressing rapidly to a fatal issue and perhaps better thought of as subacute than chronic nephritis. In these none of the methods of treatment seem to have had the slightest effect on the course of the disease; that is to say—knowledge of a close association with an infection, so far, in this group, has not shown the way to a successful treatment."

The fact that various forms of nephritis can be produced experi-

<sup>17</sup> Journal of the American Medical Association, 1920, No. 24, lxxiv, 1615.

mentally in various animals by many different bacteria and bacterial products has long been established. Streptococcus, staphylococcus, colon bacillus and diphtheria toxin, among others, have all been employed in the production of renal disease in animals. The type of lesion produced is usually a glomerular one; but associated with the glomerular involvement there may be found varying degrees of tubular and interstitial change. Many of the renal changes thus produced are anatomically similar to certain forms of nephritis seen in man and are accompanied by albuminuria and cylindruria. There has been little or no attempt, however, to correlate these types of experimental renal lesion with complete and systematic functional studies.

There is also a striking lack of investigation of the functional changes in the well-recognized infectious nephropathies seen in man. A recent article by Baehr and Lande,<sup>18</sup> calls attention to the relatively common occurrence of glomerular nephritis associated with streptococcus endocarditis. In a series of 77 cases of this disease, they have observed 9 cases who died with symptoms of uremia or other evidences of a well-marked nephritis. All these patients came to autopsy and revealed two distinct types of renal lesion:

1. "Acute Glomerulonephritis"—in two of the patients the pathological picture being identical with that seen after scarlet fever or streptococcus angina. "No bacterial emboli were demonstrable in the glomerular lesions."

2. "Chronic Diffuse Nephritis"—in 7 of the cases. "The kidney presented the gross appearance of the secondary contracted kidney and microscopically showed the typical picture of the end-stage of a chronic diffuse nephritis."

The authors do not believe that the streptococcus is the direct cause of the lesions observed, because in the "acute cases" they did not find streptococci in the glomeruli. Baehr and Lande also add that in 6 cases of subacute bacterial endocarditis due to the *Bacillus influenza* there was no evidence of nephritis.

I have always been impressed with the fact that many cases of streptococcus endocarditis showed clinical evidence of nephritis—particularly in the late stages of the disease. Functional tests in several cases seen at the Presbyterian Hospital during the last few years have revealed definite evidence of renal insufficiency—albumin, casts and nitrogen retention—are frequent findings, as is also edema and anemia. The latter two symptoms, of course, may be due partly, at least, to the general wasting caused by the blood infection.

Moschcowitz<sup>19</sup> presents a rather interesting theory of the etiology of the majority of cases of nephritis. The arguments used to support his theory are based upon certain anatomic and clinical observations coupled with certain theoretical deductions. The author's basic hypothesis is that the genesis of most of the nephritides is arteriosclerosis and that the latter finding is almost invariably accompanied by hypertension.

<sup>18</sup> Journal of the American Medical Association, 1920, No. 12, lxxv, 789.

<sup>19</sup> Archives of Internal Medicine, 1920, No. 3, xxvi, 259.

Moschcowitz also offers a new classification of chronic renal disease. Following are his conclusions:

"1. Clinical findings in nephritis cannot be interpreted in terms of morphologic pathology, except to only a very limited degree. This is due to (a) various extrarenal factors; (b) to the fact that the 'type' of the kidney as found at necropsy does not represent an end-product but a stage in a fairly well defined pathogenesis. The lesion begins as a glomerulonephritis and all subsequent stages down to the contracted kidney can be traced and are explainable, according to established genetic and morphologic criteria, from this lesion.

2. Thus the conception is set forth that chronic nephritis is essentially a vascular disease, beginning in the capillaries (glomeruli) and extending therefrom to the larger bloodvessels. The term "arteriocapillary fibrosis" devised by Sutton and Gull, appears to fit the nature of the malady better than any in current use. In this light chronic nephritis and arteriosclerosis are one and the same lesion. Arteriosclerosis is conceived not as a disease affecting only the larger vessels, but of the entire arterial system from the capillaries to the aorta.

3. The lesions in albuminuric retinitis are analogous morphologically with those of chronic nephritis. This analogy and the sequential relation of albuminuric retinitis to hypertension is a strong argument in favor of the previously submitted thesis that nephritis is not the primary cause of hypertension but is a secondary consequence to the hypertension itself or of the cause or causes (unknown) of the hypertension.

4. The presence or extent of albuminuria bears no consistent relationship to the degree or variety of anatomic destruction of the kidney. Physiologic conditions are more important factors in causing albuminuria than anatomic disturbances in the kidney.

5. The presence or degree of hypertension bears no consistent relationship to the degree or variety of anatomic destruction of the kidney. The probability is very strong that clinically cases of chronic nephritis begin as cases of "essential hypertension." If patients with essential hypertension are followed over a long period of time there progressively develops the clinical evidence of either generalized arteriosclerosis, localized arteriosclerosis (cerebral endarteritis, coronary sclerosis, albuminuric retinitis) or renal arteriocapillary fibrosis (chronic nephritis) or a combination of these.

6. The only variety of chronic nephritis that can be reasonably termed an end-result is the so-called "contracted" kidney. The contracted kidney arising from a chronic glomerulonephritis (secondary contracted kidney) is morphologically indistinguishable from the "primary contracted" kidney. A "contracted" kidney may be unassociated with hypertension, left ventricular hypertrophy or evidences of renal insufficiency. In such instances, the patient does not die a "renal" death. The kidney is termed the "decreased" kidney since it corresponds clinically to the "decreased" variety of arteriosclerosis described by Allbutt.

7. The most important extrarenal factor in modifying renal insufficiency in "arteriocapillary fibrosis" is circulatory insufficiency. Other



things being equal, improvement in circulatory insufficiency is coördinate with improvement in renal insufficiency, and *vice versa*.

8. There is a striking parallelism between the signs of renal insufficiency in arteriocardillary fibrosis associated with hypertension and those noted in frank valvular lesions of the heart. Decompensated phases of valvular heart disease may show evidences of renal insufficiency indistinguishable from those witnessed in chronic nephritis.

As a consequence of these studies the following clinical pathologic classification of chronic nephritis is submitted.

1. Arteriocardillary fibrosis.
2. Chronic glomerulonephritis or subacute bacterial endocarditis.
3. Amyloid kidney.
4. "Chronic parenchymatous nephritis" or nephrosis (Epstein).

In PROGRESSIVE MEDICINE for 1918, Christian<sup>20</sup> mentions a type of chronic renal disease described by Epstein, in which there was a marked decrease of the total protein of blood serum and a relative increase in the globulin fraction, this latter phenomenon, Epstein asserts, is due to the continual loss of albumin through the urine. The patients show marked edema and are of that type of nephritis usually spoken of as "Chronic Parenchymatous Nephritis." Epstein calls this type of nephritis the "Econdocrinic" or "Metabolic" type of "Parenchymatous Nephritis."

Kahn,<sup>21</sup> in a series of 37 cases of renal disease, of which 23 are of the "chronic parenchymatous" type, found no cases with a decrease in the protein content of the blood—such as described by Epstein—nor did he find any "marked" disturbance in the albumin-globulin ratio. He contends that if such cases exist they must be exceedingly rare. Epstein also claims that in these cases there exists a marked increase in the cholesterol content of the blood. Kahn's comment on this is as follows:

"So far as the cholesterol content of the serum is concerned one can only say that while in general there is an increase of this lipin in the blood serum in cases of parenchymatous nephritis, this is by no means a universal rule. It must also be observed that the cholesterol content is increased by certain other conditions as for example: 'In chronic interstitial nephritis, in diseases with serous effusions (at times) and in certain metabolic derangements.'"

My own experience during the past three years with cases of the type described by Epstein is in accord with that of Kahn. Bauman, working in the wards of the Presbyterian Hospital, has studied two patients who corresponded clinically to the Epstein type and they both showed a high cholesterol content of the blood and a globulin to albumin ratio similar to those found in Epstein's cases. One case, a child of five years, had considerable edema and an attempt to relieve this by high protein feeding resulted in a gastro-intestinal disturbance and had to be abandoned. On a low salt diet this patient improved slightly. In the second case the edema had largely disappeared on admission to the hospital, and continued salt restriction alone soon caused the remaining edema to disappear. Eight other cases clinically similar to those described by

<sup>20</sup> PROGRESSIVE MEDICINE, 1918, No. 4, vol. xxi.

<sup>21</sup> Archives of Internal Medicine, 1920, No. 1, xxv, 112.

Epstein have been observed where salt and fluid restriction caused the edema to disappear. Unfortunately no blood protein or blood cholesterol determinations were made.

In an article entitled "*Urinary Tract Purpura*," Stevens<sup>22</sup> and Peters describe a new clinical entity. This is an acute febrile disease with hematuria, urinary frequency, dysuria and differing from ordinary hemorrhagic nephritis (acute) in the absence, for the most part, of edema. It is probably a new disease entity, though cases that fit well into this new clinical syndrome are found scattered sparsely through the literature. In the past the cases have been confused with other similar conditions, such as acute nephritis, and without the aid of cystoscopy the condition as an entity might not have been identified. The bladder picture, however, is almost typical, with numerous submucous hemorrhages and blood streaming out of both ureteral orifices.

There is usually no history of predisposing factors. The onset for the most part is sudden, sometimes preceded for a day or two by headache, pains in the legs, malaise, weakness and vertigo. In a small number of cases the patient may have malaise for as long as a week preceding the acute onset, but the onset of the conditions even in these cases is usually acute.

The symptoms of onset are, prostration, malaise, headache, pains in the legs, gross hematuria, pollakiuria, dysuria and pyrexia. In the early stage the general appearance is that of one suffering with an acute infection, later pallor and general debility are the most striking features. The common signs of nephritis are absent, edema, dyspnea and uremic manifestations being extremely infrequent.

There were two types of pain present, the general body pains and headaches, and the pains referable to the urinary tract, the latter varying from a dull ache over the lumbar region to sharp pains not unlike those of renal colic.

Weakness and dizziness were rather frequent. Herpes labialis was noted in a few cases. A few patients had a transient cardiac enlargement, but in none was the blood-pressure elevated. In a few cases there was tenderness over the kidney region. Pyrexia was almost universally present, being rather irregular in type, rather high at onset, falling rapidly and continuing a low, irregular, intermittent course for some time after the acute onset. The pulse was elevated and often stayed elevated after the temperature had reached normal.

The urinary findings were gross blood, casts (usually hyaline and granular), occasionally leukocytes and only very faint traces of albumin. The gross blood cleared rather rapidly but microscopically could be found for long periods. There was a diminished output of phenolsulphonephthalein which usually improved with convalescence. Bacteriological studies were practically negative.

The blood revealed very little. There was no leukocytosis but late in the disease a slight secondary anemia occurred. Blood cultures revealed nothing.

<sup>22</sup> Journal of Urology, 1920, No. 1, iv, 1.

The bladder picture was quite striking, with hemorrhages in the bladder mucosa varying from a few to over one hundred in number, irregular in outline and from the size of a petechial spot 1 cm. in diameter, chiefly found on the posterior wall, sometimes involving the trigone. When gross hematuria was found at the time of cystoscopy blood was usually seen coming out of both ureteral orifices. The subsequent cystoscopic examination revealed that the hemorrhages were absorbed rather rapidly and that new hemorrhages could occur. From snared off bladder tissue studied microscopically nothing was revealed. Some cases that clinically fitted into this condition revealed nothing in the bladder, but it is reasonable to suppose that the purpura only affected the ureters and kidneys.

As far as has been observed the disease runs a long course, with occasional acute relapses. The findings of these authors of a possible new clinical entity should stimulate cystoscopic investigation in all cases of acute nephritis with hematuria.

**SYPHILIS AND NEPHRITIS.** Thompson<sup>23</sup> believes that the evidence of syphilis of the kidney is of less frequent occurrence than has been commonly supposed. He summarizes the types as follows:

1. (a) Transient albuminuria probably not due to invasion of the spirochetes.

- (b) Acute or subacute nephritis (the lesions in the kidney resembling those seen in acute nephritis).

(Spirochetes have been demonstrated in kidney tissue of these cases.) Tubular degeneration, interstitial infiltration and endarteritis and rarely glomerular involvement are found. In the subacute type the glomeruli are more frequently involved.

2. (a) Later involvement.

- (b) Chronic interstitial and parenchymatous nephritis is commonly found. These types are pathologically the same as in the ordinary nephritides, amyloid kidneys are also seen and the spirochetæ have been demonstrated in the kidney tissue. Gummata of the kidney are very rare. They occur as simple or multiple gummata, at times, presenting a sclerogummatous condition. With the cases of transient albuminuria there are no typical symptoms. These cases of transient albuminuria would probably be recognized more frequently if repeated examinations of the urine were made in early syphilis. The acute nephritis of syphilis can occur before the appearance of skin lesions or as late as three years after the primary chancre. The onset is insidious, starting with edema which may develop very rapidly. Anorexia and pyrexia occur. The urinary findings are similar to those observed in other forms of acute nephritis, the striking things being the large amount of albuminuria and the doubly refractive lipoids found in the epithelial cells. Renal function is less interfered with than in other types of acute nephritis. The appearance of chronic nephritis, which may appear later and after the primary infection, is of comparatively rare occurrence. The symptoms and urinary findings depend on the type of nephritis found.

<sup>23</sup> Journal of the American Medical Association, 1920, No. 1, vol. lxxv.



Amyloid changes are also apt to occur late and they are characterized by the symptoms of amyloid kidneys due to other causes. Gummata also occur late in the course of the disease rarely before the fourth to fifth year. The diagnosis of this latter condition is usually aided by the appearance of other syphilitic manifestations or by a positive Wassermann test. The cases of chronic nephritis are very difficult to differentiate from other cases of chronic nephritis.

The prognosis of the transient albuminuria is good and it yields rapidly to treatment. The cases of acute nephritis offer a more serious prognosis but usually under careful handling recovery is complete. The cases of the chronic type yield favorably to anti-syphilitic therapy.

Bauman and Hansman<sup>24</sup> report a case of nephritis with lipuria unassociated with fistulous tracts connecting the lymphatic system with some portions of the urinary tract—this latter condition giving rise to the well known condition chyluria—usually associated with filariasis. The present authors therefore believe that the fat, found in the urine of their case and a few other similar cases already reported, to be due to increased permeability of the tubular epithelium for fat. They assert that usually the kidney excretes an average of 8.5 mg. of fat per day and that 73 mg. per day is reported in one case of parenchymatous nephritis. Fat excretion in the case reported by Bauman and Hansman was over 100 mg. after a fat meal. No figures are given for the total of fat excretion during a twenty-four-hour period. It is suggested that this condition (lipuria) may be invariably associated with luetic nephritis, Stengel and Austin having frequently found doubly refractile bodies in the urine of nephritic patients with syphilis.

The anti-luetic treatment of cases of nephritis thought to be due to syphilis demands a word of caution. Clinically, it is not an uncommon occurrence to find nephritis due to other causes than syphilis associated with general lues and in that case the administration of mercury or salvarsan may cause further damage to the kidneys. When such a condition as the above is suspected it is wise to begin treatment with iodides alone, and then cautiously add mercury—the use of the latter drug being carefully controlled by (1) daily observations upon changes in the degree of albuminuria and (2) by frequent determinations of kidney function.

**SEVERE EXERCISE.** It has been known that severe muscular exercise will produce a certain degree of irritation of the kidney. This is evidenced by the appearance of albumin and casts in the urine.

Barach,<sup>25</sup> working on 24 young men who had completed a marathon run of twenty-four miles, found that 19 of these individuals showed albumen and casts in their urine, while 18 also showed red blood cells, and an increased urinary acidity. From another group of 57 individuals, where the exercise engaged in was less severe, Barach found that albuminuria and cylindruria were produced with equal facility, whether the exercise was mild or severe, and that the long periods of exercise had no more effect upon the production of albuminuria and cylindruria than did the exercise periods of shorter duration. He also concluded that the in-

<sup>24</sup> Journal of the American Medical Association, 1920, No. 20, lxxiv, 1375.

<sup>25</sup> American Journal of the Medical Sciences, 1920, No. 3, clxx, 398.

creased urinary acidity is not a factor in the productions of these changes in the urine.

**TREATMENT.** Any consideration of the treatment of nephritis is most satisfactorily outlined under the following general headings:

1. Diet.
2. Fluids and Salt.
3. General Hygienic Procedures.
4. Drugs.

Under the first heading we have to deal principally with the restriction or proper regulation of the protein intake. The purpose of such a procedure is in the main, two-fold:

(a) To relieve the kidney of overstrain, particularly when there is a retention of the non-protein nitrogen in the blood.

(b) To alleviate hypertension and its concomitant symptoms. Protein restriction of itself is very often not effective in lowering blood-pressure in cases of nephritis with hypertension, particularly when there is no retention of urea. When to protein,<sup>26</sup> restriction, is added the restriction of salt and fluids—a marked lowering of blood-pressure often ensues, even without rest in bed. It would, therefore, seem that a combination of salt, fluid and protein restriction together with a certain degree of under-feeding is more effective in lowering blood-pressure than is the restriction of either salt, fluid or protein alone.

The following brief summary of a case of nephritis will illustrate the effect of protein restriction upon urea retention, clinical symptoms, hypertension and phthalein excretion.

A man, aged fifty-nine years, who has suffered from vertigo, headache and precordial oppression, was admitted to the Presbyterian Hospital in October, 1918. His blood pressure was 210/100. The arteries were slightly sclerotic, the heart was enlarged to the left and there was slight pretibial edema. The blood uric acid was 6 mg. per 100 c.c., the blood urea was .085 grams per 100 c.c., and the creatinin 1.8 mg. per 100 c.c. of blood. The phthalein (two hours) was 25 per cent., the urine contained albumin, casts and occasional red blood cells, the salt concentration of the twenty-four-hour specimen was 3 grams per liter. The total output of salt on a non-restricted intake was ten grams in twenty-four hours. The urine was of low and fixed specific gravity. It was estimated on admission that this individual's protein intake amounted to somewhere between eighty and one hundred grams. The patient was put on a low protein diet (30 grams), with 7 grams of salt and two weeks later the blood-pressure had fallen to 170/90, the blood urea had dropped to .035 per cent., the phenolphthalein excretion was 45 per cent. and there was no edema. It was subsequently found after a long period of trial diets that the patient could take 60 grams of protein without an accumulation of urea in the blood, although 80 grams, if given even for a week, promptly produced an increase in the blood urea. With the above improvement in the functional findings there was also noted a corresponding improvement in subjective symptoms. This patient was

<sup>26</sup> The protein restriction alluded to is only intended to apply to those cases where there is evidence of urea retention.

observed for one year on a protein intake which was not above 60 grams per day and his functional tests at the end of that time differed only slightly from those performed when he was discharged from the hospital, and the symptomatic relief was maintained. The effect of treatment in this case demonstrates the value of continued supervision of the diet controlled by determinations of the urea in the blood.

In these cases of nephritis with urea retention the question often presents itself. To what extent should the protein be restricted? This answer is not always an easy one. Broadly speaking and without any certain method to govern us, it may be said that the restriction necessary in a given case is that required to affect a marked reduction of the urea in the blood. Thirty grams of protein per day is an intake which, in the large majority of instances, will lower the blood urea to a normal, or nearly normal level. In a few of the more advanced cases of nephritis a much more marked restriction of protein, down to 1 to 5 grams per day, may in some instances lower a high blood urea which has been resistant to a less marked restriction of protein. An instance of a case where the protein intake was maintained at less than 1 gram per day for seven days and immediately following this a period of eleven days in which the protein intake averaged less than ten grams per day, with the consequent lowering of the blood urea from 105 mg. per 100 c.c. blood to 63 mg. per 100 c.c. of blood, is cited by Allen.<sup>27</sup> This author, in two articles dealing with hypertension associated with nephritis and nephritis associated with diabetes, emphasizes the importance of extreme restriction of protein in cases with persistent urea retention. He also believes that the same extreme restriction of salt (to the limit of an actually salt-free diet) when long continued is usually effective in lowering the blood-pressure in even the most stubborn cases of hypertension with or without nephritis. Protein restriction while it is also advised in many of these cases of hypertension is only advised in the presence of a high blood urea, the high blood-pressure being "affected only through the salt and water functions."

That Allen was actually able to reduce the protein in some cases of nephritis to less than 5 gms. per day is evidenced by the fact that the output of nitrogen in the urine was often maintained for days at a level of 1 to 4 gms. (for most of the time in a given case it was below 3 gms.). The loss of weight that follows such a method of treatment is considerable and the physical weakness produced is marked in many cases.

In nephritis, there can be no doubt of the fact that extreme loss of weight due to the undernutrition usually accompanying protein starvation, and the loss of salt to the body due to salt restriction is successful in reducing blood-pressure and in relieving subjective symptoms. Whether or not this condition of protein and salt starvation is permanently of any help in arresting the progress of the renal disease is questionable. Of course, as Allen suggests, the relief of overstrain of the kidneys must be of benefit to the patient and probably arrests, at least temporarily, the progress of the disease. But on the other hand, if the

<sup>27</sup> Journal of the American Medical Association, 1920, No. 10, lxxiv, 652; *Ibid.*, 1920, No. 7, lxxv, 444.



kidney is exerting any attempt at repair, is it not possible that the long-continued general under-nutrition and particularly the protein under-nutrition will include not only the starvation effects upon the other tissues of the body but also the parenchyma of the kidney itself and eventually establish a condition unfavorable to a regenerative process, in direct proportion to the degree of under-nutrition existing?

It will also be wise to remember that the extreme salt and protein starvation employed by Allen, as the author himself indicates, is not always permanently effective in keeping the blood-pressure at a lower level and in reducing a high plasma chloride or a high blood urea to normal.

In view of our lack of knowledge of the relation of protein metabolites to cellular activity, to oxidation changes in the tissues and to osmotic phenomena in general, it is possible that the extreme curtailment of the protein intake in certain cases of nephritis may effect such a change in the physical and chemical balances within the body as to be actually harmful and thereby produce a more rapid progression of the renal lesions.

It is well recognized that protein restriction in certain forms of renal disease when there is no nitrogen retention and when the blood-pressure is not high, is often carried to unnecessary extremes. No apparent effect is to be expected from protein restriction under such conditions as mentioned and in these cases, a protein intake of 70 to 90 grams per day is usually well tolerated and is all the more permissible when the patient is under supervision and conditions are such as to permit of periodic estimations of the non-protein nitrogen in the blood. In certain types of nephritis (Epstein) over-feeding of protein would seem to be indicated.

Many physicians are accustomed to limit the kind of protein eaten, the so-called "red meats" being especially interdicted. There is absolutely no valid evidence, clinical or experimental, to show that "red meats" are any more harmful than any other form of protein and the sooner this therapeutic fallacy is abandoned the better it will be. To forbid "red meats" is simply a rough method of controlling the total protein intake.

FLUIDS AND SALTS. 1. *Effect of Restriction upon Hypertension.* Allen, in two articles alluded to above, has emphasized the importance of extreme salt and fluid restriction (the former to less than 1 gm. and the latter to less than 500 c.c.) in reducing hypertension with or without nephritis. Salt restriction as administered in the past (2 gms. per day) with or without fluid restriction has been a well-recognized method for lowering blood-pressure, but there have been many cases who have not responded to such treatment. Allen believes that many of this latter group whose symptoms and high blood-pressure persist in spite of what we have previously considered to be a maximum salt restriction, show a striking drop in blood-pressure as the result of this extreme limitation in the salt intake which he recommends. This method of treating hypertension is similar in principle to the methods employed by Allen in the treatment of diabetes. Allen calls attention to the possible harm-

ful effects of maintaining a very low fluid intake over any long period of time in cases of nephritis who have difficulty in eliminating urea, believing that retention of urea may be augmented by such a procedure and that this retention carries with it an inevitable toxic effect.

Although this method of treatment is a distinct therapeutic advance, we should emphasize the fact that it is by no means always successful in reducing blood-pressure and that the character of the diet necessary to attain such extremely low limits in salt and fluid is not an agreeable one; therefore, it is a difficult diet to administer over long periods, and if carried out over too long a period of time will result in great physical weakness.

Allen also emphasizes the fact that this extreme salt restriction is indicated by the high plasma chlorides usually found in cases with hypertension, and the subsequent lowering of these high chloride values is the result of treatment. These high plasma chlorides are found in pure hypertension or hypertension with nephritis, with or without edema.

2. *Effect of Restriction upon Edema.* In addition to its effect upon hypertension "maximal" salt restriction may also be effective in abolishing certain obstinate cases of edema.

The following brief summary of our present-day methods for treating edema may serve a useful purpose in systematizing our present knowledge and in maintaining a consistent policy in the treatment of edema, with salt retention.

*Methods of Eliminating Edema in Nephritis or in Cardiorenal Disease.*

1. Salt restricted to 2 grams per day with fluids from 1000 to 2500 c.c. permitted.

2. Salt restricted to 2 grams per day with fluids restricted to 500 to 800 c.c.

3. Salt restricted to 1 gram or less per day with fluids restricted to 200 to 500 c.c.

4. When either one of the first three method for promoting diuresis has failed, the addition of from 5 to 10 grams of salt for one day may in certain rare instances promote a striking diuresis with a marked increase in the salt output. This increased diuresis may not take place immediately (two to three days) but when it does occur it usually continues until edema has disappeared.

5. Involves the use of Method 1 or 2 plus digitalis in cardiorenal disease—when the cardiac factor in the production of edema is the dominant one.

6. Involves the use of Method 2 or 3 plus diuretics of the caffeine, Theobromine, Theocin group. Any and all of the other so-called diuretic drugs such as potassium citrate, Basham's mixture, etc., are, in my experience, wanting in any diuretic properties and are not only useless in abolishing edema but are actually harmful in some cases because of their effect upon the gastro-intestinal tract.

These diuretics should be abandoned and I am sure that the belief in their therapeutic effect has been based upon faulty observation in some instances, and in other instances has been due to failure to recognize other conditions such as salt or fluid restriction that prevailed during

the course of treatment which directly contributed to the diuretic effect obtained.

Host,<sup>28</sup> in an excellent review of the chemistry and physiology of salt metabolism, has studied 9 cases of nephritis from the standpoint of their salt and fluid exchange. He shows that in 3 out of 9 cases of acute nephritis ("glomerular nephritis"), edema existing in all, he was able to produce diuresis and increased salt elimination by several days of "low salt diet" (7 gms.) and follow this up by one day of added salt (5 to 10 gms.) whereupon there ensued the above-mentioned salt excretion. The blood serum chlorides were high until the extra salt had been eliminated and they then resumed their normal level.

No results are given for the treatment of the other 6 cases. In a summary of his own work and that of others, the author believes that "chloride retention in nephritis" can be explained on the following basis:

"1. A condition in which the chloride concentration of the blood is increased. Here the retention is mainly due to the kidneys—while extrarenal factors are of minor importance.

2. A condition in which the chlorides of the blood are not increased—the cases being due entirely to extrarenal factors."

I have seen cases of nephritis without edema and without salt retention as determined by the concentration of plasma chlorides, who show distinct loss of ability to excrete salt on an intake of 7 gms. or less. In other words, a positive salt balance exists. What becomes of this salt and where is it stored? It must be in the tissues of the body—yet why, if excess salt in the tissues is conducive to water retention in some cases, is it not capable of producing water retention in others? The answer to this question must be the fact that originally the tissues contained salt in concentration below their usual requirements. This type of case often associated with hypertension illustrates one of the many evidences that a definite disturbance in metabolism exists in nephritis in which the kidney probably plays a very minor part because many of the other evidences of deficient renal function are lacking. One cannot discount the fact that a normal or low plasma chloride level in such cases may indicate a high kidney threshold for salt and that the kidney, under such conditions, is the real barrier to the excretion of salt.

3. *Effect of Restriction upon the General Metabolism and Inorganic Salts.* The use of long-continued salt poor or salt free diets in nephritis often results in great bodily weakness, gastro-intestinal disturbance and headaches. I have observed one case of diabetes suffering from great weakness who had been kept on a "salt-free" and "starvation" diet for eight weeks or more before admission to the hospital. The only apparent reason for restricting salt in this patient had been the fact that there was considerable edema present, due in all probability to the prolonged undernutrition. Shortly after admission, while still on a salt poor diet, diuresis began and with it developed tetany.

The blood CO<sub>2</sub> was 104 volumes per cent. The patient died apparently



as the result of tetany. As there was no other demonstrable cause of tetany it was assumed that it was in some way due to the salt starvation and a concomitant disturbance of the calcium exchange. This explanation seems all the more probable because of the fact that in other patients where equally severe undernutrition has been observed but where a certain quantity of salt was administered, no other instances of tetany have occurred.

Of course it is realized that the occurrence of this isolated instance of tetany in diabetes is no proof that the same condition may occur in nephritis. This instance is quoted simply to show the possibilities of a serious disturbance in mineral metabolism due to prolonged food and salt starvation. The fact that some cases of nephritis suddenly develop uremic convulsions following a long period of diuresis with unusual salt excretion is suggestive of the fact that a disturbance of the metabolism of inorganic substances may at least indirectly, and in some cases, be responsible for the uremic state.

A very useful practical method for the regulation of the protein intake in nephritis has been advised by Walsh and O'Hare.<sup>29</sup> This is in the form of a diet sheet, and is particularly convenient for use in dispensary practice. In each group of foods the various portions contain varying amounts of protein and these amounts are listed as follows: In Group 1, each full portion contains 4 grams of protein while in Group 2, each full portion contains 8 grams of protein. In Group 3, the amount of protein present is so small that no restriction is placed upon foods in this group.

**NEPHRITIC DIET SHEET.** Any combination of the foods listed below may be selected.

Foods not listed below must not be taken.

In Group 1 and 2 there is a restriction in the total amount.

The foods in these groups must be served in full or half portions.

A full portion in Group 1 counts 1.

A full portion in Group 2 counts 2.

In Group 3, the quantity of each is not restricted, although you are urged to use discretion.

Your total score for the day should be.....

Your total amount of fluid should be.....pints.

Do not add salt or spices to the food after it has been cooked.

#### GROUP 1.—EACH FULL PORTION COUNTS 1.

	Full portion.
Bread (white) . . . . .	1 av. slice
Bread (graham) . . . . .	1 av. slice
Uneeda biscuit . . . . .	5 crackers
Shredded wheat . . . . .	1 biscuit

#### CEREALS.

Oatmeal . . . . .	2 tbsp.
Boiled rice . . . . .	3 tbsp.
Cornmeal mush . . . . .	4 tbsp.
Cream of wheat . . . . .	6 tbsp.
Farina . . . . .	6 tbsp.

<sup>29</sup> The American Journal of the Medical Sciences, 1920, No. 6, clix, 883.

## VEGETABLES.

Baked beans . . . . .	1 tbsp.
Lima beans . . . . .	1½ tbsp.
Potato, creamed (P. B. B.) . . . . .	1 tbsp.
Potato, mashed (P. B. B.) . . . . .	1½ tbsp.
Potato, boiled . . . . .	1½ med.
Green peas . . . . .	2 tbsp.
Canned corn . . . . .	2½ tbsp.
Onion, boiled . . . . .	3 tbsp.
Macaroni . . . . .	4½ tbsp.
Squash, boiled . . . . .	5½ tbsp.

## GROUP 2.—EACH FULL PORTION COUNTS 2.

	Full portion.
Milk . . . . .	1 glass
Egg . . . . .	1 egg
Eggs (scrambled) . . . . .	1½ tbsp.
Custard (P. B. B.) . . . . .	3 tbsp.

## FISH.

Cod, boiled . . . . .	1" x 1" x 1¼"
Haddock, boiled . . . . .	1½" x 1" x 1"
Oysters . . . . .	7 oysters

## MEATS.

Chicken, roast . . . . .	3" x 3" x ½"
Lamb chop, broiled . . . . .	<sup>2</sup> / <sub>3</sub> " chop
Lamb, roast . . . . .	3" x 2½" x ¼"
Beef, roast . . . . .	3" x 2" x ¼"
Beef steak, broiled . . . . .	2" x 1" x 1"

## GROUP 3.—NO RESTRICTION.

Vegetables.	Fruit.	Miscellaneous.
Turnips	Watermelon	Sugar
Carrots	Plums	Syrup
Cabbage	Pears	Candy
String beans	Peaches	Honey
Cucumbers	Strawberries	Maple sugar
Cauliflower	Grapes	Butter
Celery	Raspberries	Cornstarch
Tomato (fresh)	Blueberries	Arrowroot
Tomato (cooked)	Muskmelon	Tapioca
Lettuce	Apple	Post toastics
Asparagus	Pineapple	Maple syrup
	Prunes	Olive oil
	Apple sauce	
	Orange	
	Grape-fruit	

Cheese, which is a favorite source of protein among certain classes of ignorant patients has been omitted from this list.

Of course no diet sheet method of treatment in either diabetes or nephritis can supplant the method of individual instruction in the matter of accuracy of estimating food intake.

Individual instruction should include weighing of the food on gram scales and the use of food tables. The continued use of such a laborious procedure is not advocated for most patients because with practice, over two or three weeks, in weighing food, most people become so proficient at estimating the weight with the eye that the scales can be abandoned. Having once acquired this ability to regulate their protein accurately "by the eye" they can readily extend the range of their choice of foods.

This method of individual instruction as outlined is time consuming and cannot be applied to patients with a very low order of intelligence, but if accurate restriction of food is therapeutically necessary the time spent in instruction is well worth while.

In this connection it is well to realize that a surprisingly large number of individuals who are otherwise poorly endowed intellectually, are capable of comprehending instruction in dietetics.

TREATMENT OF HYPERTENSION. Moschcowitz,<sup>30</sup> in a discussion of the treatment of hypertension with or without evidence of nephritis, divides the treatment into four subheadings:

1. *Instructions to Patients*, in which he advocates the importance of not making the patients constantly aware of the symptom, high blood-pressure.

2. *Diet*. He sees no reason here for limiting the total amount of protein eaten but makes no mention of the fact that control of this by means of blood urea determination is of value. He strongly advises general restriction of food with the end in view of producing a mild degree of under-nutrition.

3. *Exercise*. Under this heading golf particularly is advised, or some similar form of exercise, but nothing of a more strenuous nature. Rest is rarely indicated. The author claims that this method of treatment often renders the patient's mental condition worse, without affecting any permanent results upon the blood-pressure.

4. *Drugs*. This is a general discussion of the usual drugs used in hypertension such as iodides, nitrites, etc. Moschcowitz finds that they are rarely of any use except in the case of iodides. The latter he believes should only be used when syphilis is suspected. Digitalis, however, is one drug that may be of great value in the treatment of hypertension. Other drugs are useless and may do harm.

The author believes that most cases of hypertension are primary and he judges improvement by the effect of any treatment upon the systolic and the diastolic blood-pressure, particularly the latter—digitalis being especially useful in accomplishing a beneficial result when administered to those cases where there is definite evidence of an overworked heart, as evidenced by increased pulse-rate, precordial oppression, etc., or when mild symptoms of decompensation are present, the effect of the treatment being controlled by frequent blood-pressure determinations.

<sup>30</sup> The American Journal of the Medical Sciences, 1920, No. 4, cliv, 517.



# GENITO-URINARY DISEASES.

BY CHARLES W. BONNEY, M.D.

## DISEASES OF THE KIDNEYS AND URETERS.

**Renal Tumors.** One of the most fatal affections to which childhood is subject is the renal neoplasm known as ADENOSARCOMA, or mixed tumor. In the vast majority of cases, this neoplasm affects children of tender age, rarely developing in those who have passed the eighth year. According to Albarran and Imbert, whose work on renal tumors still remains a classic, 152 out of a total of 165 cases which they collected occurred during the first seven years of life. So rare is this neoplasm in adolescence and in adult life that it is invariably thought of as one peculiar to early childhood. A few scattering cases, however, have been reported in patients varying from eighteen to fifty-five years of age. The death-rate following operation, as well as that due to recurrences, is high, the former, according to a series of cases submitted by different surgeons, varying from about 20 to more than 50 per cent. As in all forms of malignant disease, the secret of successful treatment is early diagnosis and early operation. Late diagnosis and late operation invariably mean death from metastases to other parts of the body.

In a recent exhaustive study of these neoplasms, John Fraser,<sup>1</sup> of Edinburgh, reports 7 cases which occurred in his service at the Children's Hospital in that city during a period of about two and one-half years. In 3 of these cases, operation was contra-indicated on account of the extension of the growth. In the 4 cases in which a nephrectomy was performed, there was no postoperative mortality; but at the time of the publication of the author's report, only one of the patients was living, all the others having succumbed to the effects of metastases in other parts of the body. Two years had elapsed since operation upon the patient who was still alive.

Fraser discusses the etiology, symptomatology, pathology, diagnosis and treatment in a painstaking and thorough manner. As the hypothesis which he submits in explanation of the cause of these tumors is based upon their pathology, it will be considered in conjunction with their morbid anatomy, the clinical symptoms being taken up first. The latter, as observed by Fraser, may be summarized as follows:

While the child is well nourished, active and apparently healthy, a gradual increase in the size of the abdomen is noticed. Coincidentally with this observation, it is generally recognized that the child is beginning to suffer with constipation. The abdominal swelling increases slowly, but steadily, and, in the course of a short time, a well-defined mass is

<sup>1</sup> Edinburgh Medical Journal, June, 1920.

discovered in the region of the kidney. At this stage, the general health may have been so well maintained that the child's parents are loath to believe anything very serious is the matter with it, and hesitate about having an operation performed. If there is much delay, however, the symptoms become greatly aggravated. The swelling increases very rapidly; the superficial abdominal veins become distended; the constipation yields less readily to cathartics; and the child rapidly becomes emaciated, and shows very plainly that he is seriously ill. Later, ascites develops, the limbs swell, and death ensues as the result of cachexia or of an infiltrative or metastatic growth in some vital organ. The end may be hastened by an intercurrent affection, of which bronchopneumonia is probably the most common. The author states that in well-developed tumors of this type, blood is not present in the urine. He maintains that there is no channel through which the blood from the tumor may find its way out, inasmuch as the growth of the neoplasm leads to the disappearance of the calices, the obliteration of the renal pelvis and, finally, to occlusion of the upper end of the ureter.

In discussing diagnosis, Fraser mentions certain conditions which may simulate renal neoplasm, although he lays stress upon the probability that any rapidly growing tumor in the lumbar region of a child, associated with emaciation and cachexia, usually means a tumor of the kidney. Malignant disease of the retroperitoneal lymph nodes is more centrally located. Hydronephrosis is very rare in children, as are also tumors of the liver, so that the differentiation of either of these conditions should not give rise to any difficulty. Splenic enlargement might be confused with a tumor of the left kidney, although in doubtful cases an examination of the blood will frequently lead to the correct diagnosis. Furthermore, the sharp anterior border of the spleen is likely to impart a different feeling to the palpating finger from that imparted by the upper rounded pole of the kidney. It will also be helpful to remember that the colon does not pass in front of the spleen.

All the tumors which Fraser removed were most carefully examined microscopically by the block method, the advantage of which, as the author particularly states, is to give a pictorial idea of the distribution of the tumor's tissues and the changes which these tissues undergo. A median coronal section of the entire kidney was made in two parallel planes. A model of this was accurately made from thick paper, and the tissue was subdivided into a number of blocks, as nearly as possible equal in size. These blocks were numbered and their position noted upon the accompanying model. Each block was then sectioned and examined microscopically, and the appearances recorded on the key. In this way, a microscopical picture representative of the mesial section of the entire kidney was obtained.

Six different varieties of tissue are met with in a tumor of a moderate degree of development: Renal tissue, adenomatous tissue, sarcomatous tissue, unstriped muscular tissue, connective tissue and vascular tissue. The renal tissue is gradually displaced by the tumor formation, so that it eventually appears as a thin cap-like area upon both poles of the tumor. The adenomatous tissue forms the original tumor. It develops

within the interior of the kidney, and the author believes that it takes origin from a group of nephrogenetic cells, which, instead of developing into the tubules of the kidney, take on an erratic growth, and so give rise to the adenomatous tissue of the tumor. He believes, furthermore, that such erratic growth is dependent upon an error in the development of the renal vessels. In all his specimens the bloodvessels seemed imperfectly developed. The main renal artery was small. From it there was a distribution of the blood to the poles of the kidney, the center of the growth being very imperfectly supplied. The adenomatous tissue does not infiltrate the substance of the kidney, but gradually pushes it aside. The sarcomatous tissue, the author believes, results from metaplasia of the adenomatous tissue, the change beginning in the center of the latter, and gradually extending until sarcoma formation has completely replaced all the adenomatous tissue. The non-striped muscle is derived from the muscular tissue which normally occurs in the renal pelvis. Its distribution is limited to an area in the center of the mesial edge, although, in the more extensive growths, the infiltration of tumor tissue produces a wide separation of groups of muscle fibers. The bloodvessels remain of a primitive structure. While the tumor is in the adenomatous stage, the degree of vascularity is small. With the beginning of the sarcomatous change, however, the vascularity greatly increases. From these considerations, it is seen that the neoplasm undergoes an evolutionary change from a tumor of low malignancy to one of high malignancy. In comparing the pathological findings with the symptom-complex, one can readily understand how it is that in the early stages of its evolution, this neoplasm gives rise to comparatively trifling symptoms; and also how it is that sudden changes in the patient's general condition manifest themselves when the tumor breaks through its confining wall and infiltrates the kidney and contiguous structures. Dissemination may also take place through the blood-stream, forming metastases in remote parts of the body. The tumor tissue which is disseminated in this manner may be either adenomatous or sarcomatous. It is noteworthy, however, that when an adenomatous metastasis occurs it eventually undergoes a conversion into sarcoma. Secondary deposits have been found in the opposite kidney, in the liver, in the lungs and in the central nervous system.

All of Fraser's patients who were suitable for operation were subjected to abdominal nephrectomy. He has found that the Trendelenburg position makes the operation easier; and he also favors it because it preserves the blood in the vital organs of the body, and thus helps to lessen postoperative shock. When nodulation of the tumor is found at operation, the prognosis is considered very grave, for nodulation indicates that the sarcomatous change in the interior has begun to make its way to the surface, and perhaps has already involved contiguous structures.

While discussing MALIGNANT RENAL TUMORS, the case of a patient whom Ravasini<sup>2</sup> presented at the meeting of the Italian Surgical Society

<sup>2</sup> *La Riforma Medica*, October 18, October 23 and November 1, 1919.



in October, 1919, may be worthy of narration. It was that of a man, aged sixty-three years, upon whom Ravasini operated in 1907. The patient had his first attack of hematuria, which lasted for a day, in 1906. The second attack came on a year later, and was followed by complete retention of urine, due to filling of the bladder with clots. He was taken to the hospital, and, upon examination, an unusually large mass was found in his right flank. Operation was performed, and, after some difficulty, the tumor was removed. Despite the fact that two ribs had to be resected, that both the pleura and the peritoneum were accidentally opened, and that all the tissues were considerably traumatized, the wound healed by first intention. The tumor, which was as large as a child's head, was found to be a hypernephroma. At the time Ravasini presented this patient before the society, twelve years had elapsed since the operation; and during all of that period the patient had enjoyed the best of health. In discussing this case, the author stated that another patient upon whom he had operated for hypernephroma had died two years after the operation from metastasis to the other kidney. He also took occasion, during the course of his remarks, to mention some statistics concerning freedom from recurrence after operations for malignant renal tumors. He mentioned a patient operated on by Krönlein who was free from recurrence after twenty years; two by Israel who were known to have remained well eleven and fifteen years, respectively; and one by Quénu who was well at the expiration of twenty years. He finally called attention to Forgue's collection of 28 cases in which there had been no recurrence for more than four years.

Michaelson<sup>3</sup> reports the results obtained in a series of 30 cases of HYPERNEPHROMA which he operated upon between the years 1896 and 1915. Thus it is seen that the postoperative observation period was at least four years. At the time his report was made, only 7 of the patients were alive; 4 died at the time of operation, 6 succumbed to recurrence within three years after the operation, and 3 to recurrence more than three years after the operation. Of the remaining 10, 5 died within eighteen months after the operation of some other disease, and the remaining 5 had succumbed to other affections at variable periods of time since the operation. Comparing his own experience with the experience of other surgeons who have published reports on hypernephroma, Michaelson has formed the opinion that the malignancy of this neoplasm has been somewhat underrated. This error he attributes particularly to the circumstance that some surgeons have accepted a three-year period of freedom from recurrence as indicative of cure. In this connection he calls attention to the fact that one of his patients died of recurrence ten years after operation. Referring to microscopic examinations made in the majority of his cases, he states that it is very difficult to determine the degree of malignancy of a new growth by a study of its histologic characteristics. In a few cases, however, there seemed to be some correlation between the histologic and clinical signs of malignancy.

<sup>3</sup> *Hygiea*, April 7, 1920.

**Renal Tuberculosis.** Among the most important papers which have come to my attention during the last few years is one by Braasch<sup>4</sup> based on the vast material of the Mayo Clinic and comprising 532 cases operated upon from January 1, 1894, to January 1, 1918.

The author makes prognosis the principal topic of his analysis, basing it upon age, sex, tuberculosis in other organs of the body, duration of symptoms, degree of involvement of the bladder and kidney and, finally, upon bilateral disease. The greatest incidence of surgical renal tuberculosis was in patients between the ages of twenty and forty, the largest number of cases affecting those in the third decade of life. Concerning its incidence in children, the records of the clinic show that renal lesions are almost invariably associated with a more or less extensive dissemination of tuberculosis throughout other organs of the body. With regard to the influence of age upon ultimate prognosis, it would seem, from examination of this large number of cases, that it exerts scarcely any influence. In the first and last decades of life there are too few cases to warrant the drawing of any positive conclusions. In common with other series of cases, this series shows males to be much more susceptible than females, almost twice as many men being affected as women.

Especially interesting are the facts relating to associated lesions. Out of 346 cases of the total number studied, evidence of lesions in other parts of the body, either healed or active, were found in 244 cases. In explanation of this proportion it may be stated that since 1912 more accurate records were kept than in the preceding years, and that the 346 cases studied in this connection had come under treatment since that year. So common is this association that Braasch expresses doubt whether renal tuberculosis ever occurs without there being associated lesions in other organs of the body. That such complications exert but little influence upon the final prognosis, is shown by the mortality percentage in this series, which, strange as it may seem, was somewhat lower than that noted in the general average of patients submitted to operation. Furthermore, it is interesting to note that the percentage of recovery was relatively as great when multiple lesions were present as when only one lesion was present, the single exception to this statement applying to active complications which existed in conjunction with generalized tuberculosis. Of the more common associated lesions, pulmonary tuberculosis requires some discussion. It would seem that it usually is found as a chronic process, healing of active lesions having taken place or being well under way. In 300 cases the physical examination was supplemented by a complete x-ray study. In this group evidence of pulmonary involvement was found in 84 (28 per cent.); a variety of lesions were detected, varying from active destruction of lung tissue with cavity formation to slight morbid tissue changes, which in some cases were revealed only as suspicious shadows during the fluoroscopic examination. Sixteen patients who were suffering from definite active lesions in the lungs were operated upon and, as might be expected, the mortality rate was high, 6 of the number succumbing. Despite this

<sup>4</sup> American Journal of the Medical Sciences, January, 1920.



unfortunate outcome, Braasch does not consider active pulmonary tuberculosis to be a distinct contra-indication in every case. Naturally, account must be taken of the extent to which it is present in each individual. In several of the cases above referred to, the general condition of the patients distinctly favored operation, despite the fact that they suffered from extensive lesions in one or both lungs. None of these patients died in the hospital or shortly after they were discharged, and this circumstance leads Braasch to infer that the effect of ether upon pulmonary lesions is not as harmful as some have held it to be. With regard to involvement of the genitalia in male patients, it was found that various organs were affected in 171 out of 234 cases. The late mortality was not greatly influenced by these complications, and it is worth bearing in mind that in this large series of cases lesions in the prostate and seminal vesicles showed a marked tendency to heal after the affected kidney had been removed, and that consequently Braasch advises against secondary operations upon these organs. He does, however, advise surgical treatment for disease of the epididymis and testicle, because of the tendency which lesions in those organs have to undergo exacerbations, and also because their removal extirpates foci from which other lesions may originate. Epididymectomy was performed fifty times, 26 of the operations being done before the kidney was removed and 24 after the latter organ had been taken out. There were 21 patients who suffered from associated disease of the bones or joints, irrespective of 14 who had developed spondylitis. Although active disease in the spine makes the prognosis more grave, it does not of itself contra-indicate operation. One of the patients with an active process who was operated upon six years ago is still living and in fairly good health. When the disease has become chronic it does not seem to have any influence upon the prognosis, either immediate or remote. Among patients with marked bladder involvement the mortality was twice as high as it was among those who had only slight vesical lesions. Likewise, it was found that the mortality rate was greatly influenced by the degree of destruction which the kidney itself had undergone. In this series of cases it was highest among those patients who had developed pyonephrosis. Occluded renal tuberculosis is indicative of a relative immunity and a low mortality.

In discussing bilateral disease, the author states that the end-results in this series of cases, 16 in number, do not corroborate the opinions sometimes expressed that removal of the more diseased kidney will exert a beneficial influence upon the other organ. That some improvement may result because of the lessened toxemia resulting from the removal of one kidney the author does not deny. He does not recommend operation in these cases unless one kidney has undergone almost complete destruction while the other one is still in fair condition. Under no circumstances should hope of eventual recovery be entertained.

With regard to mortality, it may be stated that death during or immediately after operation occurs so rarely that it is considered a negligible factor. The late mortality, that is, five years or somewhat less after operation, was about 20 per cent. in this large series of cases. Failure to effect complete cure is approximately 20 per cent. This leaves a



prognosis of recovery in 80 per cent. of all cases. Complete cure was obtained in 60 per cent.

As stated when renal tuberculosis was last discussed in this review, the watch-word should be *early diagnosis and early operation*. I cannot refrain from repeating that every patient who is affected with vesical irritability and has purulent urine should be subjected to a complete cystoscopic and radiographic examination if the symptoms, both subjective and objective, do not yield promptly to simple therapeutic measures. In all such cases a microscopic examination of the urine, properly centrifugized, should be made as soon as the patient comes under observation.

In a recent article on the prophylaxis of renal tuberculosis, Taddei<sup>5</sup> states that every young person whose urine shows albumin, pus or blood, and who has not previously suffered from any infectious disease, should at once be suspected of having a tuberculous kidney even if his general health is good. It has been this author's experience, in common with that of many other surgeons, to find that the subjects of renal tuberculosis have been treated for other diseases. For example, he mentions intestinal intoxication, gastritis, rheumatism and typhoid fever. In many such cases the urine had not even been looked at. In others it was merely tested for albumin, the presence of the latter leading to a diagnosis of mild nephritis. The thought that the albuminous reaction was dependent on pus apparently never occurred to the unfortunate patients' medical attendants. Taddei calls attention to the fact that very little attention has been given to this form of tuberculosis by Public Health and Antituberculosis Societies and he makes a plea for a more general dissemination of knowledge concerning this manifestation of the disease.

A knowledge of the *structural and functional conditions of the non-affected kidney* in the course of renal tuberculosis is a matter of prime importance and, naturally, has constituted the subject of numerous investigations. Among the more recent of these may be mentioned the work of G. Forni,<sup>6</sup> based upon ten experiments performed upon guinea-pigs and rabbits. After infecting one kidney of these animals, he removed the organ on the opposite side and examined it by making serial sections. From fifteen to ninety days were allowed to elapse in the cases of different animals before the sound kidney was removed.

Forni summarizes his findings as follows: In the glomeruli, a capillary hyperemia was found, with an increase of cell nuclei and vacuolar degeneration of the epithelium. Bowman's capsules were dilated and showed cloudy swelling. The epithelium of the convoluted tubules was swollen, the outline of the cells being indistinct; and in the advanced cases, there was some desquamation of the epithelium. Hyaline and epithelial casts were also frequently noted. The straight tubules presented the same changes, although they were less pronounced. In the interstitial tissue, foci resembling primitive tubercles were observed. Many lymphocytes were also seen, but the tubercle bacillus could not be demonstrated. Thus it is seen that a glomerulo-tubular parenchymatous nephritis had been set up, together with a mild interstitial inflammation.

<sup>5</sup> La Riforma Medica, November 29, 1919.

<sup>6</sup> Bollettino delle Scienze Mediche, November, 1919.

In discussing these tissue changes, Forni asks whether these lesions are to be considered specific (that is, whether they are caused by the bacillus of Koch), or whether they are to be considered as secondary toxic or infectious changes. In answer to the question, he makes the following comments: All theories that attribute the changes to a reno-renal reflex, to a sympathetic nephritis, and to the absorption of non-specific toxins from the diseased kidney cannot be accepted as essentially correct, for the reason that the conditions found in the second kidney can be reproduced in animals that have two healthy kidneys by injecting tubercle bacilli or their toxins directly into the general circulation. Furthermore, examination of multiple sections of kidneys experimentally infected with tubercle bacilli show serial changes identical with those observed at a later stage in the kidney of the opposite side. In view of these circumstances, he maintains that the morbid process set up in the second kidney is due to the action of tuberculous toxins liberated in the diseased kidney and carried to the healthy one by the blood stream. The hyperemia to which it at first gives rise naturally favors their elimination in the urine secreted by the second kidney; but, as the result of the said hyperemia, at first protective, alterations eventually take place in the renal parenchyma. A continuation of the process, as in any form of nephritis, may eventually lead to a more or less active involvement of the connective tissue of the organ. In human tuberculosis, there is ample evidence to show that the process is the same.

**Renal and Ureteral Lithiasis.** During the last year a number of important articles dealing with different aspects of renal and ureteral lithiasis have been published. With regard to *etiology*, Charles H. Mayo<sup>7</sup> expresses the opinion that the only tenable theory is that which attributes stone formation to bacterial infection. The fact that bacteria from the blood are constantly being eliminated through the kidneys would seem to render those organs very susceptible to contamination. According to Mayo, two types of microorganisms must be present in order that calculi may develop. The action of one type results in the formation of an infarct, together with minute necrosis, these changes being followed by a mucoid exudate. The second type causes elimination of the first type and thus they come in contact with the mucoid material and produce the stone. The process of stone formation may be very gradual and the patient may not have any pain until complications arise.

In discussing the management of these cases, the author states that medical treatment is founded on the principle that changes in the chemical composition of the urine may be produced by altering the diet, by drinking large quantities of water which dilute the material to be eliminated, and by bringing about the elimination of different forms of chemical and bacterial debris.

The impression which one gets by reading different articles dealing with the surgical treatment is that at present surgeons are not so anxious as they formerly were to operate as soon as a diagnosis is made. Last

<sup>7</sup> Annals of Surgery, February, 1920.



winter Keyes read a paper on urinary calculi before the Philadelphia Genito-urinary Society in which, among other things, the indications for operation were thoroughly discussed. He expressed the opinion that prompt operation for ureteral calculi is indicated only when alarming symptoms develop. He also advised surgical removal when the stone remains stationary and when it is more than 0.5 cm. in diameter.

Two other contributions have also been made by members of the Mayo brothers' staff, one by Braasch<sup>8</sup> and the other by Judd.<sup>9</sup> Braasch also believes that one should not resort too quickly to operative measures, since it has been his experience that three-fourths of the stones will pass spontaneously. He states that operation should be deferred from three to six months unless there is continued retention of urine or renal infection. This rule of course does not apply if the stone is too large to be passed. Bilateral calculi also call for prompt surgical interference. In such cases the kidney which is functioning the better should be operated upon first, although sometimes it may be practicable to operate upon both kidneys at the same time. Mayo likewise recommends immediate operation in all emergency cases, even though the kidney function is very low. In the paper by Keyes, above referred to, drainage by pyelotomy was recommended; and in cases of complete suppression of urine bilateral drainage was advised, even though stones are present in only one kidney. Among the complications discussed by Mayo are polycystic kidney, hypertrophy of the prostate and pregnancy. He states that operation may be justifiable in selected cases of polycystic diseases and that pregnancy up to the sixth month does not constitute a contra-indication. Even later in gestation their removal has been successfully accomplished. Naturally, when prostatic hypertrophy is associated with renal or ureteral lithiasis, the prostate should be operated upon before any attack is made upon the ureter or kidney.

Judd agrees with Braasch with regard to keeping the patient under observation for some time in hope that the stones will pass spontaneously. He states that manipulations through the operating cystoscope, together with administration of papaverin, has often proved successful, although he cautions against too frequent repetition of such manipulations lest they cause infection. It is evident that Judd's experience with this form of treatment is the same as those of other surgeons, in that he finds it most applicable to stones impacted in the lower portion of the ureter. If a fair trial of non-operative treatment proves fruitless, then the author believes that one should not hesitate to resort to operation. The technic, of course, will vary with the location of the stone. Only one in four hundred patients in this series of cases died as the result of operation.

In a succinct paper in which he discusses 50 cases in which he performed operations, Hugh Lett<sup>10</sup> devotes some space to a discussion of the treatment to be followed after operation, especially that which has to do with preventing the recurrence of stone. While he realizes that an

<sup>8</sup> Journal of the American Medical Association, January 4, 1920.

<sup>9</sup> Annals of Surgery, February, 1920.

<sup>10</sup> The Practitioner, August, 1920.



important cause of recurrence is incomplete removal of stones at the time of operation, he is of the opinion that faulty systemic conditions also may give rise to their formation. Consequently he instructs all his patients to pay particular attention to their diet. Milk, cheese, sugar and alcohol are forbidden and the use of hard water is also discounted. At least three pints of distilled water should be drunk every day. The bowels are kept free by means of laxatives, if necessary. A moderate amount of exercise is also prescribed.

In order to insure the removal of all stones, Lett has the x-ray plate brought to the operating room at the time of operation and checks up the number of calculi removed with those shown in the picture. He feels that the greatest danger of leaving any behind exists when soft phosphatic stones are present, for they may be broken into fragments when seized with forceps; and any débris unremoved may serve as nuclei for the formation of other stones. In such cases, therefore, he always syringes out the pelvis and calyces of the kidney in order to remove any particles which may have escaped his attention.

The mortality rate of Lett's 50 cases was low. Only 2 patients died. These were both affected with acute pyelitis, and one of them had been suffering from calculous anuria and complete suppression of urine for three days. Operation was undertaken as a forlorn hope and merely consisted of draining the pelvis of each kidney. The other patient was a woman, fifty-eight years of age, who had suffered from attacks of renal colic for ten years. At operation, one large stone and three small ones were removed from the right kidney; and although there was nothing unusual about the operation, the patient developed an acute exacerbation of a chronic colitis and died. There were 9 cases of pyonephrosis in this series, 6 of which necessitated nephrectomy. There was also one case in which a perinephric abscess had formed.

*Prolonged hemorrhage* in renal lithiasis is a subject which has received attention from Escudié.<sup>11</sup> As the bleeding which usually accompanies stone is trifling, although characteristic, severe hemorrhage may naturally lead to a mistake in diagnosis. For example, neoplasm or tuberculosis might be suspected, or even hemorrhagic nephritis. Therefore to guard against error it becomes necessary to enter carefully into the patient's past history and determine whether he has ever presented any signs of lithiasis. The anamnesis, of course, should always be supplemented by an x-ray examination, which will usually show whether stones are present. The characteristics of this form of hemorrhage are by no means alike in all cases, and it is noted by the author that they may present great diversity. For example, the bleeding sometimes came on suddenly, without any appreciable cause, and then disappeared just as abruptly as it had begun, only to start again without warning after a considerable length of time. Again, it was noted that it was just as abundant when the patient was put to rest as when he was allowed to be up and about; and that in some cases it was resistant to every form of treatment. The patient may not suffer the slightest

<sup>11</sup> Jour. d'Urol., November 5, 1919.

pain, either in the region of the kidneys or in the bladder; and, furthermore, urination may be absolutely painless, even when clots are expelled. Thus it is seen that in this class of cases the hematuria is the principal, if not the only symptom, and is one which certainly would not at first lead the surgeon to suspect the real nature of the underlying trouble. The author refers to four of these puzzling cases in which a correct diagnosis was eventually made.

In this connection, it seems proper to insist upon routine *x*-ray examination, as well as complete cystoscopy with ureteral catheterization and functional renal tests, in every case of surgical renal disease. Of course, those of us who are in the large cities possess the advantage of having such examinations made by experts. With the general improvement in hospital equipment and the more general training of young men to do special work, there are now greater facilities than ever before for having such examinations done in the smaller communities, especially those in which the hospitals are becoming standardized.

*Retrograde movement of ureteral calculi* is a rare occurrence, at least insofar as any record of cases in the literature shows. Reverse peristalsis is one condition which has been considered the cause. Another theory is that backward movement takes place when the ureter becomes dilated. A case in which the latter condition seems to have been causative has recently been reported by John H. Neff.<sup>12</sup> The patient, a female aged twenty-four years, was admitted to the hospital in July, 1919 with a diagnosis of right pyelitis. Cystoscopy revealed considerable inflammation at the base of the bladder. The urine from the left kidney was negative. An obstruction was encountered in the right ureter 2 cm. above its vesical orifice. *X*-ray examination disclosed a stone in the lower part of the right ureter. On the following day an attempt was made to dislodge the calculus by dilating and injecting olive oil. About a month later another attempt at dilatation and dislodgement of the stone was made. With the Lewis dilator the ureter was stretched to 17 French. Following this treatment, the patient had repeated chills and high fever. Two days later, upon vaginal examination, considerable induration and soreness were found at the base of the right broad ligament, and it was thought that some leakage of the urine might have taken place. A vaginal incision was made, but nothing except a non-suppurative periureteritis was found. Six weeks after this operation another *x*-ray picture of the lower urinary tract was made, but no shadow of a stone was obtained. In the interval the patient had gained considerably in weight and had been free from all symptoms. She had watched her urine carefully and felt sure that she had not passed a calculus. In view of this finding, an *x*-ray picture of the kidney was taken, with the result that a calculus was shown in the renal pelvis. The next day, operation was performed and a stone removed from one of the middle calyces. The exposed portion of the ureter was only slightly dilated, in fact so slightly that it would have been difficult to force the stone down into the ureter. The stone measured 5x7x10 mm.



Neff believes that migration of this calculus was due to the dilatation of the ureter. The sharp reaction after dilatation followed by the inflammation around the ureter, as revealed upon vaginal section, leads him to the conclusion that a complete temporary occlusion of the ureter had taken place, this occlusion being accompanied by wide dilatation above, thereby favoring ascent of the dislodged stone. He thinks that the position of the patient in bed after the first operation may have had some effect also. Ureteral instrumentation could not have carried the stone higher than four inches as no instrument was passed for a greater distance.

**Decapsulation for Nephritis.** In 1896, Reginald Harrison published a paper in which some forms of albuminuria associated with kidney tension were discussed, and pointed out that mechanical relief of the tension might prove beneficial in restoring the kidneys to normal function. He had operated for suspected suppuration of the kidneys in 3 cases in which a mistake in diagnosis had been made. One was a case of nephritis following scarlet fever; another, nephritis resulting from exposure to cold and wet; and the third, nephritis that had supervened upon an attack of influenza. In these 3 cases relief was obtained by nephrotomy and drainage. It was five years after Harrison's publication that Edebohls advised decapsulation in chronic nephritis, assuming that by stripping up the capsule of the kidney, an anastomosis could be brought about between the arteries of the cortex and those of the perirenal tissue. Although this theory was proved to be erroneous, inasmuch as postmortem examinations of kidneys that had been decapsulated for nephritis, as well as those that had been decapsulated experimentally in animals, showed them to be enclosed in an envelope of scar tissue, the operation itself has occasionally been performed, and apparently with good results. It is not in chronic nephritis, however, but in the subacute parenchymatous form of the disease, especially in children, that such results have been obtained. In this review, four years ago, the subject was discussed in connection with 25 cases reported by Lloyd, of New York, 15 of which were distinctly of the parenchymatous form.

In a recent exhaustive review of the subject, W. G. Spencer<sup>13</sup> summarizes the present status of the operation. All the evidence he has collected tends to show that the operation is useless in the chronic interstitial nephritis of adults, but that, as previously stated, it has given relief in cases of subacute parenchymatous nephritis, in some instances even when there was a complicating anasarca and ascites. In this class of cases, the decapsulation should be done as soon as it is clear that improvement does not quickly follow medical treatment. Both kidneys should be decapsulated, and preferably at the same operation. When the second decapsulation is put off, Spencer finds that greater swelling and congestion of the second kidney follows.

The question naturally arises as to what percentage of cases of acute and subacute parenchymatous nephritis will require surgical treatment. Certainly it is rare for the surgeon to be called upon to do a decapsulation.

<sup>13</sup> Medical Science, May, 1920.



In this connection, a paper by Bratke<sup>14</sup> is significant. In a summary of 149 cases of kidney diseases in children, there was not a single one that required decapsulation. Cassel,<sup>15</sup> whose experience in pediatrics has been extensive, also states, in reporting a case in which he had both kidneys of a nine-year-old girl decapsulated, that it was the first time he had had occasion to have such an operation performed.

Cassel's patient had been attacked by general dropsy and albuminuria about a month before she came under his observation. When he first saw her, she was suffering from uremia, which was at first partly relieved by medical treatment, together with venesection. The abdomen was tapped, and 2000 c.c. of fluid drawn off. Six weeks later she had another attack of uremia which resisted all treatment; therefore, on the fourth day, both kidneys were decapsulated. The perirenal tissues were edematous, the kidneys much enlarged, the capsule being very thick and readily stripped off. The day after the operation, she passed 220 c.c. of urine; and on the following day, 910 c.c. A month after the operation, it was necessary to tap her again for ascites; and a third paracentesis had to be performed three months after the second. Eleven months after the operation, however, all signs of dropsy had disappeared, and the child was in good physical condition. She was examined six years after the operation, and was found to be in good health, although there was a trace of albumin in her urine. This would seem to be the rule—good health, but persistent albuminuria of varying degree.

Spencer points out that anuria may come on as the result of infections in kidneys that have previously been sound, and cautions against decapsulation in such cases. This subject was discussed in *PROGRESSIVE MEDICINE* several years ago, Brewer's work being fully reviewed. In these cases, the treatment is either nephrotomy or nephrectomy. Spencer likewise discusses the indications for decapsulation in eclampsia and in postpartum renal infections, but that field of the operation will not receive attention here.

Another report on this subject has been made by Kümmell,<sup>16</sup> who at a recent meeting of the Hamburg Medical Society stated he had operated upon twelve soldiers suffering from war-nephritis, and that the results in every case were very gratifying. Some of these patients were uremic when the decapsulation was performed. The author also expressed the opinion that the operation may be of benefit in chronic nephritis, but in the discussion which followed his paper no one agreed with him in this respect.

**Duodenal Fistula Following Nephrectomy.** The relation of the right kidney to the duodenum is such that injuries may be inflicted upon the latter structure in removing a kidney that has become adherent to contiguous parts as the result of inflammation. The experience of William J. Mayo in this class of cases was discussed in a previous review. Last winter, two interesting cases of duodenal fistula, both of which presented rather unusual features, were reported at meetings of the French Urological Society.

<sup>14</sup> *Jahrb. f. Kinderheilk.*, 1919, No. 3.

<sup>15</sup> *Deutsch. med. Wchnschr.*, September 25, 1919.

<sup>16</sup> *Berl. med. Wchnschr.*, February 14, 1920.

The first one, reported by Michon,<sup>17</sup> was that of a woman aged thirty-five years, who entered the hospital in March, 1919, suffering with sharp abdominal pain, vomiting and fever. Upon examination, a large tumor was found in the right hypochondrium. It was diagnosed as an infected hydronephrosis and was removed without any especial difficulty. During the operation, the second portion of the duodenum was brought plainly into view, so that there was no question about having included a portion of it in the ligature placed around the pedicle. A rubber drainage-tube was inserted into the wound. One week after the operation the patient complained that her dressings were wet, and upon examination it was found that they were saturated with a yellowish, bile-like fluid. There was so much discharge that the dressings had to be changed again in the evening, and when they were examined, particles of caseous material were seen with the bile, the former being attributed to the partial digestion of milk that the patient had taken in the afternoon. There was now no doubt that a duodenal fistula had become established. The next day the lumbar incision was opened, and an attempt was made to find and suture the fistula. Despite complete opening of the wound and the most careful examination, the fistula could not be found. It was noticed, however, that the proximal end of the drainage-tube was in contact with the deepest part of the wound; and it was considered possible that the opening into the bowel might have resulted from pressure made by the tube. For this reason, the tube was removed. To his great surprise, Michon found that the discharge from the wound had diminished a great deal by evening. Within the next twenty-four hours it had completely stopped; and it did not reappear.

In this case it is evident that the connection between the bowel and the lumbar wound was very small, in that respect differing from fistula caused by sloughing of a large portion of intestinal wall which has been clamped off at the time of the nephrectomy. The patient made a good recovery, and nine months after the operation was free from any digestive disturbance.

The second case, reported by Legueu,<sup>18</sup> did not terminate as favorably as Michon's. It was that of a man who developed a duodenal fistula about a year after his kidney had been removed secondarily to an operation previously performed for right-sided perinephric abscess. Nephrectomy was decided upon because the patient suffered from a permanent urinary fistula, severe cystitis and considerable impairment of general health. At the operation, which was performed January 10, 1917, the kidney was found to be so bound down by inflammatory products that it had to be removed by *morcellement*. Although his general condition, as well as the bladder symptoms, was greatly ameliorated by the operation, the fistula persisted; and he came to the hospital every second day for dressings. In November, 1917, more than ten months after the nephrectomy, the fistula began to discharge an abundant quantity of thin yellow liquid, resembling bile. Within a few days, the patient began to complain of illness; and it was evident that he was rapidly

<sup>17</sup> Journal d'Urologie, February, 1920, No. 2, vol. ix.

<sup>18</sup> Ibid., March, 1920.



losing weight. He was admitted to the hospital, and, a few days later, a silk ligature was discharged through the fistula. It was assumed that the ligature was the one which had been placed around the pedicle of the kidney when the latter organ was removed. The patient was kept under observation for a while, and it was Legueu's intention to attempt closure of the fistula by the abdominal route. As the patient's condition became progressively worse, the operation was not undertaken. Death occurred a few weeks after he entered the hospital. At autopsy, a large hole was found in the posterior aspect of the second portion of the duodenum, establishing a communication between the cavity of the intestine and the external surface of the body by means of a fistulous tract which passed through all the intervening parts. The duodenum itself was adherent to the scar of the nephrectomy incision. No pathological changes were found in any other organ except the liver, which was enlarged and friable.

In discussing this case, Legueu expressed the opinion that the development of a fistula so long after the kidney had been removed was due to suppuration in the kidney bed, and not to inclusion of a portion of the bowel in the ligature applied to the renal pedicle. He emphasized the rapidity with which the patient's general health had become impaired after the establishment of the fistula and the consequent loss of bile from the intestine. He also expressed the opinion that further experience would be necessary to determine the best way of treating such fistulae. That the abdominal route is the one of choice, he is convinced. He likewise suggested that gastro-enterostomy, together with exclusion of the pylorus, might facilitate the healing of the repaired duodenum.

## DISEASES OF THE BLADDER.

**Vesical Disturbances of Cerebral Origin.** Although the influence of the spinal cord upon the bladder has been thoroughly worked out by physiological experimentation and clinical observation, the action which the brain exercises upon this viscus remains obscure. That it does exert some control, however, is amply shown by a number of facts which give evidence of the intervention of the will in the act of micturition. For example, voluntary beginning of the act, ability to interrupt it before the bladder is emptied, and contraction of voluntary muscles at the end of the act, all show that the brain exerts a considerable degree of control. Further evidence is furnished by the circumstance that any interruption along the conductive paths uniting the cerebral centers and those of the spinal cord, results in inability completely to empty the bladder.

Fully twenty years ago, Czylhartz and Marburg conducted experiments upon animals which led them to believe that there is a corticovesical center situated in the motor region, irritation of which produces contractions of the bladder. This center, they stated, is connected with the spinal centers by fibers derived from the cerebral peduncles. They also described a subcortical center situated in the thalamus, which is united with other centers, above and below, by conductive pathways, originating in the anterior portion of the internal capsule and the



superficial layers of the quadrageminal bodies. The presence of the latter center was later confirmed by Karpus, Freidl and Lichtenstein. Not many clinical observations in support of these theories have been recorded. Among those that have been published may be mentioned the cases of Cylhartz and Marburg, Friedman, and Goldman. The first-named of these authors saw a case in which a patient who had a cyst of the supramarginal and angular convolutions experienced some difficulty in micturition; and in the case of a patient suffering from a compound fracture of the parietal bone, Friedman observed an almost complete incontinence which supervened upon difficulty in voiding. Goldman's case was that of a woman who developed an epidural abscess from a tuberculous lesion of the left parietal bone, and who suffered from a progressive retention of urine which disappeared after the brain abscess had been opened.

More recently, Kleist<sup>19</sup> stated that he had observed constant vesical disturbances in cases of soldiers suffering from craniocerebral injuries which had produced paralysis of both lower limbs. This phenomenon led him to hypothecate the existence of a corticovesical center in the anterior central convolution, and also, perhaps, in the paracentral lobule. The absence of disturbances when only one limb was paralyzed, was explained by Kleist upon the supposition that the center on the sound side took up the work of the one upon the injured side. In the cases which he observed, bladder disturbances were of short duration, usually clearing up within two weeks. Similar experiences were reported by two other German military surgeons, Mueller and Foerster.

In a recent exhaustive study of the subject, Fritz Brüning<sup>20</sup> reviews the literature, discusses and criticises all the theories, and finally reports two cases which came under his own observation. The first one was that of a patient who developed a large gaseous cyst in the right frontal lobe as the result of a gunshot wound of the cranium. Ten days after operation, which consisted in opening and draining the cyst, the patient, who up to that time had never had any urinary trouble, developed an incontinence which persisted for fifteen days and then completely disappeared. His case was followed for two years, and during all that time he had no vesical trouble whatsoever. The second case was that of a man who was injured in the left parietal region by a fragment of shell, and who came under the author's care six months after the injury. At that time, he was affected with motor aphasia and paralysis of the right upper and both lower limbs. After the expiration of another six months, Brüning excised the cerebral cicatrix, which was still granulating, and replaced the tissue removed by a fatty transplant; the latter, in turn, was covered by a free fascial transplant and a pedunculated cutaneous flap. Ten days after the operation, an attack of retention developed and continued for twenty-four hours, after which it spontaneously subsided. Some difficulty in voiding, however, persisted for five or six days. The author is convinced that in this case there was interference with a corticovesical center. It is interesting to note, also, that the paralysis of the

<sup>19</sup> *Deutsch. Arch. f. klin. Med.*, 1918, No. 2, vol. cxxviii.

<sup>20</sup> *Arch. f. klin. Chir.*, January 29, 1920.

lower limbs was more pronounced immediately after the operation, although it became much ameliorated within a few days. Brüning is not so sure of direct participation of the cortical center in the first case, for the reason that the field of operation involved the frontal zone. He believes that changes in cerebral tension consecutive to evacuation of the large cyst exerted enough reaction upon the only slightly remote subcortical center, situated in the region of the thalamus, to interfere with its normal action upon the bladder. From a study of previously reported cases, together with his own, Brüning concludes that lesions of the cortico-vesical center give rise to retention, and that those of the subcortical thalamic center cause incontinence. Thus he accepts the theory previously promulgated by Czylhartz and Marburg. That both of these conditions of the bladder are transitory, seems to be proved by the observations of a number of different writers on the subject. For this reason, it is likely that many cases have passed unnoticed, especially among patients who sustained craniocerebral injuries during the war.

**Migrating Bladder Stone.** Barringer<sup>21</sup> reports an interesting case in which a stone ulcerated through the bladder wall and was found lodged in the rectum. The case was that of a man fifty years of age who was admitted to the hospital complaining of some rectal trouble. Examination revealed a large stone just within the sphincter. It was removed with forceps after the patient had been anesthetized, and was as large as a hen's egg, black, rough, and very much like a piece of coal. About a dozen years before the patient had had a perineal section, presumably for stricture. Ten years ago he suffered partial retention of urine and had an abscess in the perineum. At that time he was told he had a growth in the rectum. Another perineal section was performed, and since the second operation the patient had noticed at times the escape of urine from the bowel and of fecal matter from the urethra. For six months these symptoms had been constant, and he had also suffered greatly from tenesmus and from incontinence, both urinary and fecal. The nucleus of the stone was found to be a piece of bone. Nothing could be learned to throw any light upon the manner in which it had originally gained access to the bladder. The patient improved rapidly after removal of the stone.

**Hour-Glass Bladder.** John R. Caulk<sup>22</sup> reports 2 cases of this rare condition, one in a man, the other in a woman. In the first case there was complete retention of urine, which had been preceded by considerable difficulty in voiding, the patient being able to urinate with greater ease when reclining than when in the upright position. During cystoscopic examination, it was found that a bar of tissue passed transversely across the base of the bladder about three quarters of an inch behind the plane of the ureteral orifice and became lost on the lateral bladder walls. This bar divided the bladder into two cavities. An operation was performed for the removal of this band of tissue, together with a portion of the redundant mucosa. In the other case a similar bar was found about an inch back of the trigone. It passed all the way across the base

<sup>21</sup> Journal of Urology, December, 1919.

<sup>22</sup> Annals of Surgery, January, 1920.



of the bladder and fanned out on either side in such a manner as to cause a slight puckering of the lateral walls, with a distinct pouch in front and behind. The same operation was done in this case as in the first one. The results were satisfactory in both. The author expresses the opinion that simple incision of these bands would not have given satisfactory results because they involved the whole bladder wall.

**Tumors of Bladder.** In last year's review some space was given to the discussion of IRRADIATION OF MALIGNANT VESICAL TUMORS. During the present year another important communication on the subject has appeared. Clifford Morson<sup>23</sup> reviews his experience with the method and lays down certain working rules to be observed in its application. He states that the best results are to be expected when the radium is buried in the substance of the tumor, the latter being exposed by a suprapubic cystotomy. Before the radium is introduced the bladder is kept open a number of days and thoroughly irrigated through the wound twice daily with an antiseptic solution. This preliminary treatment is for the purpose of reducing sepsis. At the end of a week the suprapubic incision is enlarged and the radium deposits are implanted in the tumor near its periphery where the cells are undergoing the most rapid proliferation. It is in advanced cases, not amenable to cutting operations, that radium stands preëminent. It is to be distinctly understood that the author does not recommend it as a substitute for partial cystectomy when that operation is feasible.

Morson's remarks upon infection in relation to radium irradiation are interesting. Although experiments have demonstrated that the sensitiveness of the malignant cell on exposure to the rays is in direct proportion to the activity of the cells' reproductive power, the actual application of radium in infected cases in which the vitality of the cell is somewhat lessened does not give as good results as it does in cases free from infection. Experiments have shown that bacteria are very resistant to the Gamma rays of the metal and that in order to destroy them a very long exposure is required. He furthermore cites some experiments performed for the purpose of determining the effect of radium upon leukocytes, which are the most efficient enemies of pathogenic bacteria. It was found that an eight-hour exposure reduced their phagocytic power 46 per cent. and that it was possible to disintegrate them completely if the exposure was sufficiently prolonged. Thus it is seen that in the presence of infection larger doses and longer exposure will be required than in cases in which infection is not present; and also that the very agents which are most effective in neutralizing the deleterious action of the bacteria will be rendered less potent by the rays with which they are brought into contact.

A case of secondary MELANO-EPITHELIOMA OF THE BLADDER has been reported by C. G. Richards<sup>24</sup> of the Mayo Clinic, and, because of the extreme rarity of this neoplasm, the case is deemed of sufficient interest to receive notice in this review. In a careful search through the literature, the author was able to find only a single case on record. The

<sup>23</sup> British Journal of Surgery, July, 1920.

<sup>24</sup> Surgery, Gynecology and Obstetrics, September, 1919.



history of Richard's patient is as follows: He was a man, aged forty-five years, who was referred to the clinic by his physician because of an enlargement of the inguinal lymph nodes which came on a short time after the removal of a pigmented mole on the abdomen. The patient stated that his mother died of cancer of the stomach at the age of seventy-three, and that she, like the patient himself, had had a number of pigmented moles distributed over various regions of the body. The mole which had been removed from Richard's patient began to enlarge about two months before it was excised. It also showed a tendency to bleed upon the slightest irritation. After he was admitted to the clinic, one of the inguinal lymph nodes was removed and, upon microscopic examination, proved to be malignant. For that reason all the lymph nodes in both groins and in Scarpa's triangle were dissected out. While the patient was convalescing from the operation, radium treatment was begun and continued at regular intervals. Eight months later a mass developed in the inguinal region which proved to be of the same structure as the enlarged nodes which had been previously removed. Later the man developed some frequency of micturition, and his urine was found to contain pus and blood. Cystoscopic examination revealed multiple areas of black, rounded tumors varying in size from 2 to 5 cm. They were on the right side of the base of the bladder and anterior to the right ureteral orifice. On the left wall there were two similar growths which were all pedunculated. Intravesical radium treatment was at once begun, but at the latest cystoscopic examination, made about a month before the publication of the case report, they had not undergone any diminution in size.

Nicolich<sup>25</sup> reports the case of a man, aged eighty years, upon whom he performed a subtotal resection of the bladder for a tumor which was plainly perceptible upon rectal examination and suprapubic palpation, and which was accompanied by abundant hematuria. At operation, it was found that the neoplasm occupied the greater part of the vesical cavity, infiltrating its walls and, at one point, involving the peritoneum. The trigonum, however, had been spared. The patient made a good operative recovery, the wound being completely healed by the fiftieth day, and the patient being able to pass his urine without difficulty. Microscopic examination of the neoplasm showed it to be a squamous-celled epithelioma, in parts of which keratinization was noted. At the time that Nicolich showed this patient before the Italian Surgical Society, nearly eight years after the operation, the patient urinated normally and, despite his great age, was able to do hard work in the fields. An x-ray picture, taken after the bladder had been injected with collargol, distinctly showed that the vesical cavity had been reconstructed by a gradual process of dilatation. In another case that the author mentioned, the result was not so felicitous, the patient having succumbed, a year after the operation, to pyelonephritis. In this case an autopsy was obtained, and evidence was found of reconstruction of the bladder by secondary dilatation.

<sup>25</sup> *La Riforma Medica*, October 18, October 23 and November 1, 1919.

**Exstrophy of the Bladder.** C. C. Holman<sup>26</sup> reports a case of exstrophy of the bladder in a boy of eight, which was successfully treated by implantation of the ureters into the rectum. On March 15, 1918, under general anesthesia, a catheter was passed into each ureter for about three inches, and then tied in place. A median incision into the bladder, supplemented by a circular incision around each ureteral opening, was made. The ureters were then dissected free, and a curved forceps was introduced into the lower bowel and pressed against the anterior rectal wall below the peritoneal reflection. After a small incision had been made over the point of these forceps, the latter was passed through and made to grasp the right ureter, together with a catheter which had previously been inserted into it. Then the two together were pulled down into the rectum. The wound in the rectum was closed by one stitch, which was also carried into the wall of the ureter. The same procedure was repeated on the left side. The remainder of the bladder was next trimmed away and the wound left open. The catheters were taken out of the ureters at the completion of the operation. The patient's general condition remained good, although he had some fever for two weeks. On March 17, the bowels acted spontaneously; and by the 19th, the boy could keep dry during the day. On April 6, there was thought to be some leakage of urine through the wound. On April 17, the granulations were cut away, and the skin edges undercut and united. Both ureters could be felt projecting into the rectum. The wound healed by first intention, and there was no leakage of urine. When the case was reported, nearly two years after operation, the patient's general health was good. He had lost control over his urine, which he was voiding two or three times during the night, and at intervals of three or four hours during the day. The operation scar was found healthy. This operation is similar to that of Peters, first described a number of years ago, differing from it only in the circumstances that the ureters were fixed by a stitch into the rectum and that the catheters were removed at the conclusion of the operation. The author states that there was probably some slight infection of the kidneys in his case, as shown by irregular pyrexia and by thirst. He also states that it might have been better if he had allowed an interval of several weeks to elapse before transplanting the left ureter, as suggested by Mayo a short time ago. The subject of implantation of the ureters into the bowel was fully reviewed in *PROGRESSIVE MEDICINE* a number of years ago; and it was conclusively shown—at least, so I believe—that infection of the kidney always takes place.

### DISEASES OF THE PROSTATE.

**Results of Prostatectomy.** Although the functional results of prostatectomy have been thoroughly investigated, less attention has been given to studying the structural results. In a recent paper on the latter subject, Phelip,<sup>27</sup> of Lyons, analyzes a few contributions which he has found scattered through the literature, and includes some unpublished

<sup>26</sup> British Medical Journal, January 31, 1920.

<sup>27</sup> Jour. d'Urologie, November 5, 1919.



investigations which his chief, Rochet, has conducted. The information which he has collected was obtained by a number of different methods, including postmortem examination, cystoscopy, urethroscopy, radiology, and a study of conditions found in patients who had been subjected to secondary operations after prostatectomy. Nearly all the patients were examined two or three months after operation, although, in some cases, a number of years had elapsed since the prostatectomy had been performed. One series of cases comprises those in which there were no operative or postoperative complications. In these it was found that the large cavity left by enucleation of the prostate had generally disappeared after a few months. In a very few, however, a considerable space was unobliterated after the expiration of a number of years. It is in this latter class that urethroscopic and cystoscopic examinations show the presence of a partition of variable dimensions between the prostatic bed and the bladder. In these cases, the *ensemble* constituted by the bladder and the prostatic bed is compared by the author to a gourd or hour-glass. It is after suprapubic prostatectomy that this condition is generally found. More frequently, however, the prostatic cavity becomes obliterated and the bladder merges with the urethra in the form of a tunnel or infundibulum. This condition is accounted for by avulsion of the prostatic urethra during removal of the prostate. Occasionally, at the level of the new internal urinary meatus, evidences of irregular contraction of the tissues are seen, although true strictures are rare. The latter, when present, will prove amenable to progressive dilatation. In general, the permeability of the urethra is amply assured. The ejaculatory ducts are preserved in the majority of cases, at least, following transvesical prostatectomy. Phelip believes, however, that they are usually destroyed in the perineal operation.

In a study of cases in which there were operative or postoperative complications, it is interesting to note that the author found only 2 cases following the perineal operation in which there were persistent vesico-rectal fistulæ. Injury to the rectum, however, during the operation was not uncommon. In a certain number of cases, a sort of regeneration of the prostate was in evidence. This condition, according to the author, is due to the liberation of a considerable portion of prostatic tissue which had previously been pushed out of place and compressed by adenomata developing from the pericervical glands. In such cases, recurrences of urinary disturbances are to be expected, inasmuch as the primary tumor has not been completely removed. In some of these "regenerated prostates," malignant degeneration has been known to occur. The greater percentage of recurrences after the perineal operation is believed to be due to the circumstance that that procedure is reserved for the removal of sclerotic, adherent prostates. With regard to the secondary procedures, it was found that progressive dilatation, internal urethrotomy, and cutting operations designed to remove diaphragm-like outgrowths in the region of the vesical neck, were all required. Furthermore, operations for the closure of hypogastric, perineal, and urethro-rectal fistulæ had to be done. For the most part, all of these various operations gave good results.



J. Thompson Walker<sup>28</sup> in a discursive paper on suprapubic prostatectomy also devotes considerable space to the study of postoperative obstruction, and recommends a modification of technic for the purpose of overcoming some forms of such obstruction. Nodules of gland substance, together with tags or flaps of mucous membrane, have been found to give

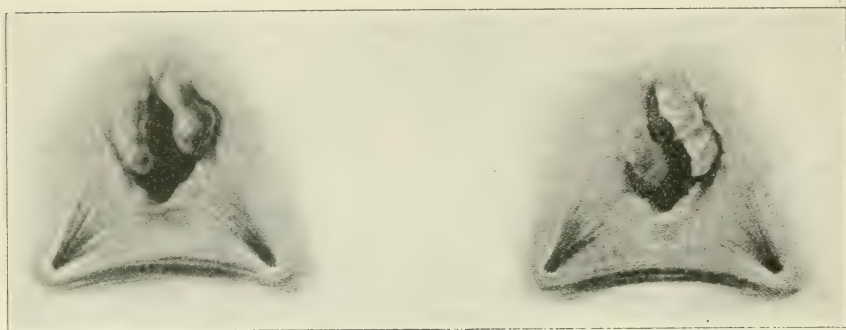


FIG. 15.—Nodules of parasitic tissues at the prostaticovesical opening (Walker.)

FIG. 16.—Strips of mucous membrane at the prostaticovesical opening. (Walker.)

rise to interference with micturition, and according to the author a large variety of them may be left after a prostatectomy. At the vesicoprostatic opening a large, loose flap of mucous membrane is frequently seen on either side, and a long strip of membrane has sometimes been seen at the anterior margin of the opening. The posterior lip of the orifice may consist of a prominent semilunar ledge, which tends to reduce the

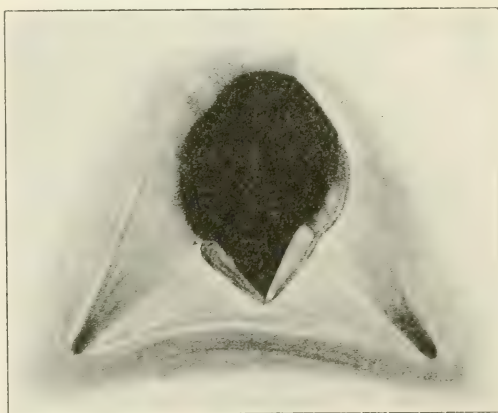


FIG. 17.—Prostaticovesical opening with wedges cut in posterior fold. (Walker.)

lumen as the cavity contracts, and may occasionally completely occlude the orifice. This ledge is formed by the trigone and the adjoining base of the bladder, and is produced by the enucleation of that part of the prostate which extends posteriorly under the base of the bladder. Loose

<sup>28</sup> British Journal of Surgery, April, 1920.

strips of the capsule of the prostate, as well as nodules of prostatic tissue which have been left behind, may also give rise to urinary obstruction when healing has taken place. Finally the author states that long loose strips of the urethral wall, which have been pulled out during enucleation of the gland, may unite with the other raw surfaces and cause obstruction. Walker takes special care to remove all such loose tags, shreds and semi-detached nodules of prostatic tissue, and also cuts a wedge-shaped piece, having its base forward, out of the posterior margin of the prostatovesical opening. The tissue removed consists of mucous membrane, muscle and frequently some glandular tissue. The length of time spent in the operation, including careful control of hemorrhage by ligation of all spurting vessels and the introduction of hemostatic stitches at the brim of the prostatic cavity, is usually about thirty minutes; and Walker states that he has not seen any increase in shock due to prolongation of the operation. If these precautions be taken, it is the author's opinion that there will be fewer unsatisfactory functional results after prostatectomy.

In cases in which the operation has been incomplete and in which obstruction is taking place, relief may be afforded the patient if the condition is recognized early. Difficulty in passing the catheter, together with difficulty in washing through the catheter and out of the wound, and delay in healing of the wound, are all indicative of this trouble. In this stage there may not be complete obstruction, so that some urine will be passed through the urethra even if the point of the catheter is arrested before it reaches the cavity of the bladder. If such a condition is recognized at an early stage, it is easy to slip the finger along the partly healed wound and meet the tip of the catheter, which can then be forced through the spot where the opening should be, now detected as a dimple or a bud of soft granulation tissue. Once the channel has been made in this manner, sounds of increasing size are passed, and then a large rubber catheter is tied in for a week or ten days. If the condition has not been recognized sufficiently early, a complete opening of the bladder is necessary to correct it. Two cases of the latter kind are cited.

One was that of a man, aged sixty-four years, who suffered from nocturnal frequency. His prostate was enlarged and he had six ounces of residual urine. In November, 1917, the prostate was removed by another surgeon. The patient began to void urine three weeks after the operation. Catheters were passed, but there was difficulty in getting them into the bladder, and finally their passage became impossible. The suprapubic wound remained open, and the urine passed partly through the urethra and partly through the fistula. In February, 1918, the same surgeon operated again. The bladder was opened and a catheter passed into the urethra and tied there. The wound healed but broke down again, and there were recurring periods of leakage from the suprapubic opening. Micturition was very difficult, and the catheter met with obstruction at the neck of the bladder the same as before. At times complete retention occurred. On April 29, 1918, Walker reoperated upon the patient, removing the suprapubic scar and freely

opening the bladder. The vesicoprostatic opening was reduced to a small aperture, which tightly gripped a small curved catheter. It was surrounded by a thick cuff of hard, fibrous tissue, more prominent on the right side. The subjoining prostatic cavity was covered by a canopy of mucous membrane and fibrous tissue, the urethral opening being at its anterior margin. All of this tissue was cut away, exposing the prostatic cavity, which was funnel-shaped. The bladder was drained. On May 10 the wound was nearly healed and the urine was passed partly through the wound and partly through the urethra. At this time a catheter could be passed with ease. In July, 1918, the patient was reported to be free from all urinary disturbance, the wound being thoroughly closed and micturition normal.

The details of the second case were similar to those just narrated. Upon opening the bladder at secondary operation, Walker found that the prostatic cavity was completely closed by a thick membrane. No opening from the bladder into the urethra could be found. A metal sound, passed along the urethra, raised up this canopy and it was caught with a pair of vulsellum forceps and a piece cut out. The opening was then extended by cutting away the remains of the cavity, and a large passage leading from the bladder into the funnel-shaped prostatic cavity was entered. A month later the suprapubic wound was healed and the urine was passed naturally.

Wishard and Hamer<sup>29</sup> have published an analysis of 120 cases of prostatic hypertrophy in which prostatectomy was performed. Two patients died in the hospital shortly after operation and four died after leaving the hospital. The authors attribute the improvement in the mortality statistics in this series to the fact that patients are now seeking relief earlier in the evolution of their urinary disturbance. Modern methods of determining each patient's operability are employed in every case which comes under the authors' care, and the procedure chosen is adapted to the requirements of the individual. Those in good condition are not subjected to the two-stage operation; eighty-seven of the operations, however, were done in two stages. Hemorrhage has been carefully controlled by a variety of methods: Packing with gauze, ligation of bleeding points, insertion of the Hagner bag, etc. Of late greater care has also been given to postoperative treatment and to nursing. The suprapubic operation was used in all of these cases.

Barringer<sup>30</sup> describes a simple method which he has found useful for controlling hemorrhage after suprapubic prostatectomy. As soon as the prostate has been enucleated, a strip of gauze several yards long is packed into the space previously occupied by the gland, pressure being made upward with two fingers of the left hand previously inserted into the rectum to facilitate enucleation. Enough of the gauze is used to distend the prostatic cavity. When the hemorrhage has been controlled, a spong-stick is passed into the bladder and the gauze grasped by it. The margins of the vesical wound are then sutured to the rectus fascia and the hole in the bladder is sewed up, just enough space being left

<sup>29</sup> Journal of the Indiana State Medical Association, 1920, p. 111.

<sup>30</sup> Journal of Urology, December, 1919.



for the gauze and sponge-stick. No drainage tubes are used, but the dressings are changed as often as they become saturated. If bleeding begins again, it is controlled by making pressure on the sponge-stick.

The advantages claimed for the method are the rapidity with which it can be executed, the necessity of only ordinary instruments and the promptness with which hemorrhage, either primary or secondary, is controlled. As disadvantages he mentions the circumstance that the patient is made uncomfortable by the constantly leaking urine and that he suffers some pain and tenesmus as the result of the pressure of the packing. It has been suggested that pressure of the packing upon the lower portion of the ureters might interfere with the flow of urine from the kidneys to the bladder, but in none of the 50 cases in which the author has used the method did any such phenomenon occur. Keyes, however, had one case in which the kidneys did not functionate until the packing was removed, but this may just as likely have been due to reflex action as to direct pressure upon the ureters.

**Sarcoma of the Prostate.** In reporting a case which occurred in his practice, F. C. Herrick,<sup>31</sup> of Cleveland, has taken occasion to review the literature and to summarize the clinical symptoms of the affection. Herrick's patient was a man aged thirty-three years, whose illness had begun several months before he consulted Herrick. He first noticed that some effort was required to empty his bladder, and this difficulty increased so rapidly that at the end of two weeks he was obliged to resort to the catheter for relief. For several months he catheterized himself regularly and experienced no trouble from the use of the instrument. At the time that he came under observation, he had lost twenty pounds in weight, but had been entirely free from pain. Upon rectal examination, a large, smooth mass of uniform consistency, firm, though yielding somewhat to pressure, and not tender to the touch, was found. Its borders were demarcated, but the finger could not reach above it. At operation, which was done by the suprapubic route, a mass of edematous-looking papillomata was found surrounding the internal meatus. Beneath this the main tumor could be felt. The entire mass was enucleated, leaving a large cavity, which was obliterated by the use of purse-string sutures. The patient made a good postoperative recovery. He was seen three and a half months after the operation, at which time a recurrence in the prostatic region had already taken place. His general condition, however, was good. Later, radium treatment was given him by Barringer, of New York; but it was not successful, and the patient succumbed. Death took place a little less than six months after the operation. At autopsy a large tumor was found, completely filling the pelvis. There were also metastases in the liver and a suppurative pyelonephritis.

In reviewing this subject, Herrick states that of the sixty-two cases he was able to find in the literature, nearly one-third occurred before the tenth year; three-fourths, before the fortieth year; and four-fifths, before the fiftieth year. From these considerations it may be inferred that a

<sup>31</sup> *Annals of Surgery*, February, 1920.

prostatic tumor occurring in adolescence is probably sarcoma; and also that one occurring before the fiftieth year should be thought of as possibly sarcomatous.

The most common symptom in this group of cases was obstruction of the bladder. Obstruction of the lower bowel was also common. In the younger patients pain was not a prominent symptom, although in those past fifty it was more noticeable. Many complained of a feeling of heaviness in the perineum. Rectal examination always revealed the presence of a large tumor of uniform consistency, smooth as to its surface and somewhat resistant to pressure.

As to diagnosis, the differentiation must be made from syphilis, tuberculosis and cancer. In cases of such prostatic enlargement, a history of congenital or acquired syphilis, a positive Wassermann reaction or other evidences of the existence of congenital or acquired lues, renders the therapeutic test necessary. A tuberculous prostate does not become so large as one affected with sarcoma. The former is of varying consistency in different parts, hard and nodular over some areas, and smooth and soft in other places. Associated disease of the seminal vesicles and epididymes may also be present, as well as tuberculous lesions in other parts of the body. Carcinoma usually occurs later in life than does sarcoma. It is smaller, harder, irregular in outline, and likewise frequently nodular. Finally, it may be stated that the age incidence, the rapidity of growth, the uniform elastic consistency and the early obstruction to urination strongly suggest sarcoma.

The treatment should consist in thorough extirpation of the tumor, followed by the application of radium. The prognosis, however, is very bad. Thus in all the cases studied by Herrick, there was only one in which death had not resulted from recurrences. He cites one case reported by Paschkis and Tittinger, in which twenty-one applications of radium, made at intervals of two weeks, had caused a disappearance of the growth. These authors, however, did not consider the patient cured at the time they reported the case.

A very interesting case of *lymphosarcoma* has recently been reported by William C. Quimby,<sup>32</sup> of Boston, who likewise reviews three other cases which he was able to find in the literature. Quimby's case was that of a married man, forty-one years of age, whose family history and past personal history were negative. About the middle of December, 1917, he was first troubled with frequent and painful urination. These symptoms subsided under rest and medical treatment, but returned shortly after Christmas of that year, becoming so severe that he entered a hospital for observation and further treatment. Relief was obtained within a few days and he was discharged, only to have the trouble return two days later, at which time retention occurred and he had to be catheterized. After several weeks of constant suffering, he entered the Brigham Hospital under Quimby's care. His urine then contained pus and blood, although his general appearance was good despite the fact that he had lost considerable flesh. Cystoscopy proved very pain-



ful. At the bladder outlet a number of irregular elevations, varying considerably in size and bleeding freely when touched, were seen. They seemed to be in the beginning of the prostatic urethra, surrounding the internal meatus. Examination of the prostate through the rectum showed the superior portion of the gland to be enlarged. Operation was decided upon and a few days later the prostate was exposed through a perineal incision. Nothing, however, could be found which indicated its removal. The seminal vesicles were also apparently normal. Then the bladder was opened suprapubically, whereupon a small mass of friable tissue was noticed in the prostatic urethra. A piece of this tissue was removed and examined microscopically and was found to be a lymphosarcoma, or as Quimby prefers to call it, *lymphoblastoma*. The patient's condition was not considered sufficiently good to warrant removal of his prostate at a second operation, as he had lost weight very rapidly and had become very weak. He died about three months later.

From a study of the onset and clinical course of this case and three other cases which Quimby found in the literature, it is evident that this form of tumor is highly malignant from its incipency, metastases taking place very early and leading to a fatal termination within a few months. It is noteworthy also that the local symptoms resembled those of urinary or genital infection. In Coupland's case the patient was treated in a hospital for spasmodic stricture, his symptoms coming on after a debauch. He died fifty-four days after admission. Metastases were found in the pancreas and adrenals. Kaufmann's patient had metastases in the pleura, kidneys, pancreas, lymph nodes of the neck and in the bones. It is evident that such a neoplasm is not amenable to any treatment at present known.

**Radium in the Treatment of Malignant Disease.** A further contribution to the radium therapy of malignant disease of the prostate has been made by Clifford Morson,<sup>33</sup> of London, who advises its use only in cases in which the disease has spread beyond the capsule of the gland. When the base of the bladder and the seminal vesicles have become infiltrated, however, he believes that irradiation will give better results than the extensive operation required under such conditions. His method of applying it in these cases is as follows: The patient being thoroughly anesthetized and placed in the lithotomy position, a sound is passed into the bladder and an incision made in the midline of the perineum. The tissues between the anterior wall of the rectum and the membranous urethra are separated by inserting the finger into the space between the anal canal and the membranous urethra. The lower pole of the prostate is felt with the finger as a guide, and the radium tube is inserted into the substance of the gland between the urethra in front and the rectum behind. To obviate the necessity of cutting into the tumor, the tube is made with a sharp pointed end. It would seem better to expose the prostate through a prerectal incision and perhaps to introduce a tube into each side of the neoplasm.

Morson also discusses other methods of applying radium and severely

<sup>33</sup> British Journal of Surgery, July, 1920.



criticizes its use in the rectum. It not only causes a great deal of pain and tenesmus, but may also produce serious alterations in the rectal mucosa. The mere placing of a tube of radium in the bladder instead of burying it in the substance of the neoplasm is deprecated, although not so much because of the possibility of injury to healthy bladder tissue as because of the impossibility of concentrating its action directly upon the diseased tissue. Finally, the author states that it is the type of growth which rarely gives rise to metastasis which is the one most successfully treated by the rays of radium. Therefore, in cases of malignant disease, of the bladder a good result may be expected, provided always that the remedy be applied with great care and with an exact knowledge of the effect of irradiation upon the normal tissues of the body. In discussing this subject in a previous review, it was stated that no one not thoroughly experienced in radium therapy should attempt to make the application.

**Blastomycosis of the Prostate.** A case of blastomycosis of the prostate has been reported by Parmenter and Simpson,<sup>34</sup> of Buffalo, N. Y. It was that of a man who had been affected with external and internal lesions of blastomycosis for about three years before any sign of the infection manifested itself in the genital organs. Urinary disturbances began in October, 1917, when an attack of frequency, urgency, burning and difficulty in voiding came on. Recurrences took place at intervals of about a month. When first seen by the authors, his total urine was purulent and contained blood and an abundance of prostatic shreds. Upon rectal examination the prostate was found to be much enlarged, and, owing to the infiltration, its outline was completely obliterated. The seminal vesicles were also involved. Massage yielded only a bloody discharge. Cystoscopic examination showed that the bladder was much smaller than normal, and that there was marked bullous edema of the trigone and sphincter. The posterior urethra and verumontanum were much inflamed and bled easily. Some of the prostatic ducts were occluded, while others were filled with mucopurulent secretion. No blastomycetes, however, could be detected when this secretion was examined. It was deemed inadvisable to resort to surgery. The patient returned home and was not examined by the authors for six months. At that time the prostate was found to be much smaller and its outlines were plainer. The right lobe was hard, nodular and very sensitive. The urine had become clear and bloodless, and the urinary symptoms were milder. At another examination made six months later, secretions obtained by massaging the prostate and seminal vesicles were found to contain blastomycetes. At this time applications of x-ray were begun, as it seemed that the morbid process in the genital organs had passed the acute stage. Improvement continued rapidly, so that in the course of a month both prostate and vesicles felt perfectly normal and all blastomycetes had disappeared from the secretion. The patient's skin lesions had previously yielded to x-ray treatment after resisting all other forms of therapy, and it was because of this circumstance that local applications to the prostate and vesicles were advised. In Decem-

ber, 1918, that is, six months after the *x*-ray treatment was begun, an epididymitis suddenly developed on the right side. Within two weeks the acute symptoms had subsided, although the epididymis was hard and considerably swollen. In view of the fact that the patient had no venereal infection, the trouble in the epididymis was attributed to blastomycotic infection. From December, 1918, to April, 1919, there had been no relapse, and repeated examination of the prostate and vesicular secretion failed to show any blastomycetes. When the case was reported, the *x*-ray treatment was being continued and the patient was taking a daily dose of 450 grains of potassium iodide. This case, which was referred by Dr. Grover Wende, who was treating the patient for the skin lesions, is the first one, so the authors believe, in which a diagnosis of blastomycosis of the prostate was made. In a series of autopsies upon patients who died of the disease, involvement of the prostate was mentioned four times. In a search through the literature, the authors could find only a single case in which the organisms were found in the urine. The patient died, and at autopsy multiple abscesses were found in the prostate.

#### DISEASES OF THE PENIS AND URETHRA.

**Dermoid Cyst of the Penis.** A man, twenty-six years of age, consulted E. König<sup>35</sup> concerning a pyriform tumor as large as a hazel nut situated on the anterior surface of the prepuce, between the two layers of that structure, immediately behind the frenum. This tumor was attached by a short pedicle, was elastic, and upon pressure gave distinct signs of fluctuation. The patient stated that the growth had been present as long as he could remember, and that it had continued to increase in size until he was about fifteen years of age, when it had ceased to grow or, at least, increased very little. An exploratory puncture failed to reveal the presence of fluid. The tumor was easily removed, and, upon section, was found to be filled with a thick, paste-like, yellow mass, evidently containing fat. The wall of the sac was smooth and white. Upon microscopic examination, it was found to be composed of dense connective tissue, abundantly vascularized, and covered with epithelium presenting all the characteristics of the epiderm. In its wall, no hair follicles, sebaceous glands or sweat-glands were found. Observation of this case led König to study congenital cysts of the prepuce and glans; and, as the result, he accepts the classification of Gerulanos, who divided them into dermoid (or epidermoid) cysts and adenomatous cysts. The walls of the former resemble the skin, and contain a semi-solid or nearly solid substance, similar to that of sebaceous cysts. The contents of the latter is serous and their walls are covered with one or more layers of cylindrical epithelium. The adenomatous cysts are the rarer of the two. Mixed forms, in the walls of which the two types of epithelium are found, have also been reported. The embryology of that portion of the urethra contained in the glans penis easily accounts for the development of these

<sup>35</sup> Arch. f. klin. Chir., 1920, Fasc. 2, vol. cxiii.

congenital cysts. They may be compared to the accessory channels which are sometimes met with in the terminal part of the urethra, and which are lined with epithelium of either type. The author states that these cysts are merely such accessory channels which have become closed at their two extremities.

**Hypospadias.** Nove-Josserand<sup>36</sup> describes a new one-stage operation for the cure of hypospadias and reports the results obtained in a series of 35 cases. The operation consists of three parts: Suprapubic cystotomy, preparation and insertion of a graft of skin around a carrier, and closure of the abnormally situated meatus. The bladder is opened and drained in the usual manner. Then an incision from 6 to 8 cm. is made along the inferior surface of the penis and scrotum in such a manner that the hypospadias opening is situated at its center. A flap of skin is raised upon either side, the urethra exposed, and an incision made in it down to the lower angle of the superficial wound. From the distal end of the urethral opening a trocar is inserted and pushed out through the glans penis, thus forming a channel for the graft. The trocar is withdrawn, but the cannula is left in place, so that it may be used as a guide for dilators if it becomes necessary to stretch the channel to facilitate the insertion of the graft. A ribbon graft of skin from 3 to 4 cm. in width and one-third greater in length than the length of the artificial channel is taken from the thigh. It is wound around and sutured to a Nélaton sound from 16 to 20 French in size, the cutaneous aspect being in contact with the catheter. The sound thus equipped is then drawn into the new canal by a special tunnel-sound and forceps. The posterior end of the Nélaton sound projects from the posterior end of the incision and serves as a drain. The hypospadias opening is then closed and finally the edges of the skin wound are brought into apposition by fine aluminum sutures and Galli tubes. The suture and graft carriers are removed in a week or ten days, the bladder being kept open until this time. For a while the urine is passed through the perineal portion of the incision, but the latter soon closes and the patient voids through the new urethra.

Churchman<sup>37</sup> calls attention to a case in which he obtained a very satisfactory result by employing Bucknall's operation which, according to the author, is too little known and too rarely used. It consists essentially in attaching the penis to flaps taken from the scrotum, allowing adhesions to form between them, then dissecting up the flaps in order to release the penis, and finally suturing the flaps together. This operation, although described by its originator more than a dozen years ago, has not become well known; therefore, a description of it is reproduced here. With the penis drawn up on the abdomen, and the scrotum drawn down in the opposite direction, between the thighs, a longitudinal incision is made on either side of the median raphe, an eighth of an inch from it. Each begins on the glans and is continued down the penis until opposite the misplaced urethra at its root. It is then prolonged on to the front of the scrotum for a distance equal to the length of the incision on the penis. Thus, the hypospadiac opening is situated at the center of a

<sup>36</sup> Jour. d'Urologie, January, 1920.

<sup>37</sup> Annals of Surgery, April, 1920.



strip of skin outlined by the incisions. From the extremities of these two incisions, two lateral incisions, each a quarter of an inch in length,

FIG. 18

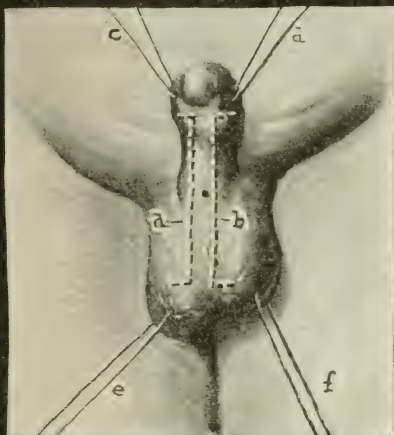


FIG. 19

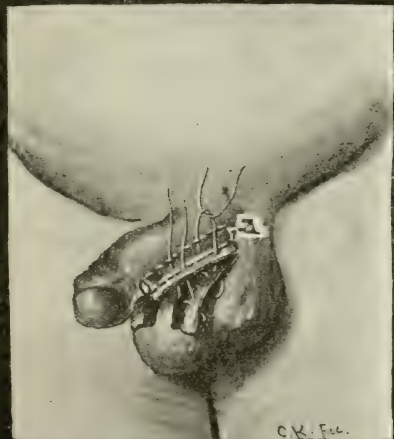
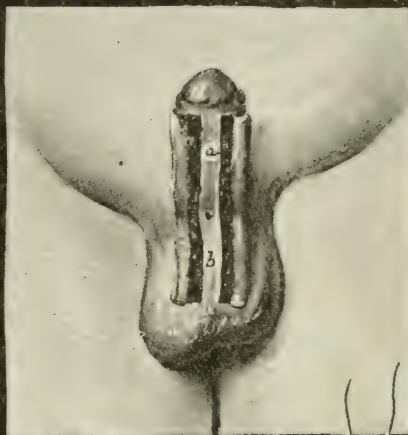


FIG. 20

FIG. 21

FIG. 18.—The first incisions are represented by dotted lines (*a* and *b*). Stay sutures hold the penis and scrotum in place (*c*, *d*, *e*, *f*).

FIG. 19.—Lateral skin flaps have been dissected up. A central strip of skin remains of which the upper or penile portion (*a*) will form the roof, the lower or scrotal portion (*b*) the floor of the new urethra.

FIG. 20.—The penis has been flexed, with the hypospadias opening as a hinge, and the lateral flaps are being sutured over rubber tubes; one of these tubes is represented by the dotted line (*a*), the corresponding rubber tube on the lower flap is omitted for purposes of clearness.

FIG. 21.—An enlarged drawing, showing the way the suture is laid, so as to approximate the skin edges (for the formation of the new urethral tube) without penetrating them. *a*, penile skin; *b*, the scrotal.

are made, and two lateral flaps are dissected up, leaving a median strip of skin untouched. Two long strips, each presenting a raw surface, are also produced by this dissection. The latter are held in the everted

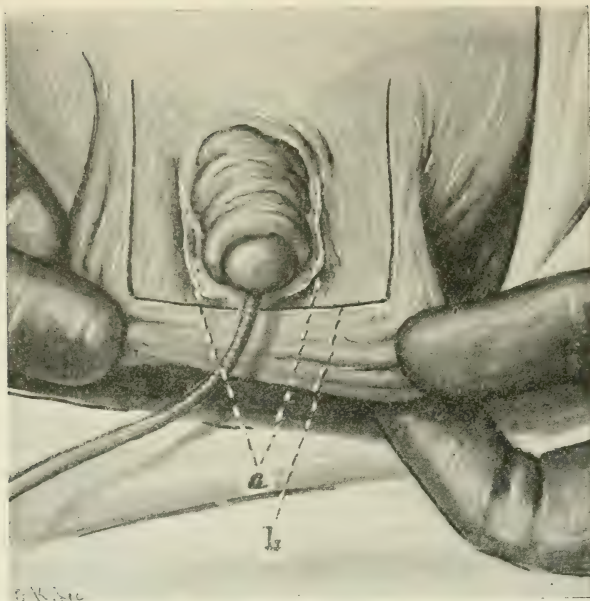


FIG. 22.—First step in the second stage operation. The penis has healed in the scrotal bed; the edges of the lateral skin flap are seen at *a*. The skin incision is shown at *b*; it is purposely represented as made further from the penis than is necessary in order to indicate that one should err on the side of lifting up too large, rather than too small, a flap. A rubber catheter has been inserted in the urethra, in order to protect it during the dissection of the penis from the scrotum.

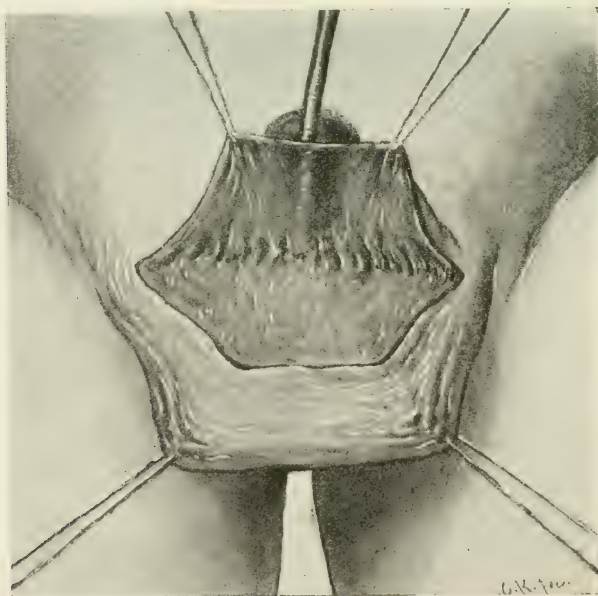


FIG. 23.—The dissection of penis from scrotum has been completed; the new urethra, distended by the catheter, can be seen bulging against the skin flap.

position with forceps throughout their entire length; and while they are in this position, the penis is flexed down on the scrotum in the middle line, so that the median strip of skin on the ventral aspect of the penis

FIG. 24

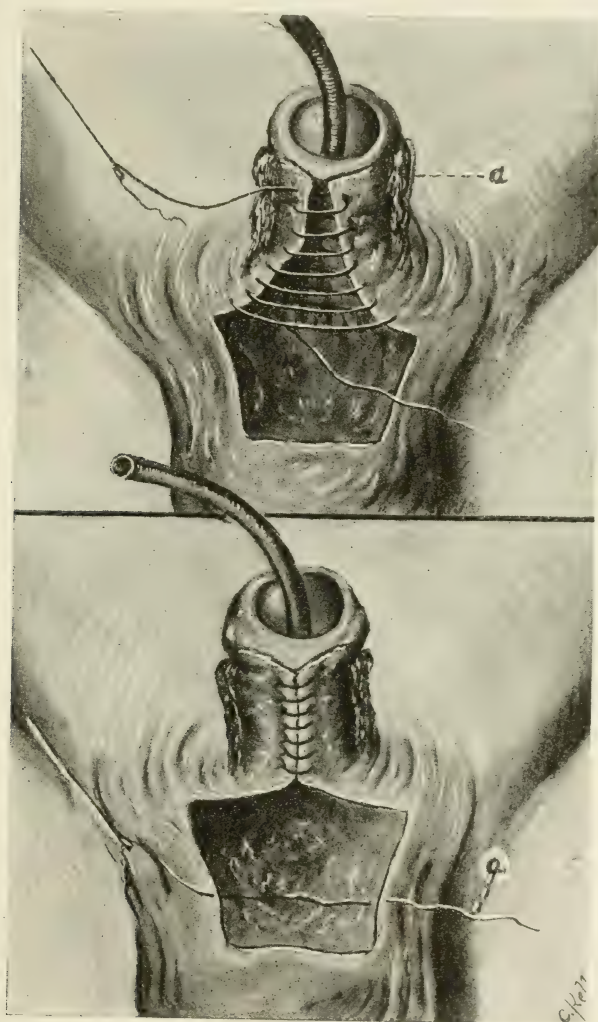


FIG. 25

FIG. 24.—Suture of scrotal flap begun; interrupted and not continuous suture as shown by the artist should be used. *a*, cutaneous wings formed by the healing of the two lateral skin flaps, sutured at the first operation.

FIG. 25.—Suture of scrotal flap completed. One suture has been placed, beginning the repair of the defect in the scrotum.

and the raw areas flanking it come into contact with the corresponding median strip and raw surfaces on the front of the scrotum. The penile strip of skin forms a roof for the new urethra and the scrotal strip forms its floor. In this position, mattress sutures are applied, being tied over



small rubber tubes. A small rubber catheter with the eye cut off is passed along the track thus formed, and which will eventually become the new urethra. It is inserted for a short distance into the hypospadiac opening, so as to drain off the urine without allowing it to come in contact with the newly constructed canal. It is held in place by a suture, passed through its distal extremity and the glans. On the fourth day the piece of catheter is removed, and the urine allowed to pass down the new urethral tube. The sutures are all taken out at the end of fourteen days, and the parts are ready for the second stage of the operation in from three to four weeks. The second stage consists in restoring the penis to its normal position and in covering over raw areas. If healing from the first operation is not complete at the end of a month, no attempt should be made to do the second stage, for healing from the first operation is essential before anything further can be undertaken. The penis and new urethra are dissected up from the scrotum, lateral flaps derived from the scrotum being left on either side of the penis to close in the raw surface beneath it. Other flaps are formed on the scrotum, and by gliding them toward the middle line, the raw surface is easily closed. If the lateral flaps used to unite the penis and scrotum in the first stage are seen to project too freely, they can be trimmed off with scissors. The accompanying illustrations should serve to make the operation plain. The object of this operation, as will be readily seen, is to advance the opening from the penoscrotal junction to the region of the glans. It is conceivable that in some cases an attempt might be made to bring the urethra out through a passage-way tunneled through the glans itself. In Churchman's case, however, the latter procedure was not deemed advisable.

**Stricture of the Urethra.** Maximilian Stern,<sup>38</sup> of New York, describes a plastic operation for the cure of stricture which he hopes may take the place of external urethrotomy. It consists essentially in a careful dissection of the structures lying in front of the urethra, so that the latter can be exposed and the strictured floor at the bulbomembranous junction excised without inflicting injury on any other parts. With the patient in the exaggerated lithotomy position, an inverted  $\Delta$  incision is made, its apex being situated about an inch above the position corresponding to the tip of the staff previously introduced into the urethra, and extending down to the stricture. The staff also carries a filiform, which passes through the stricture into the bladder, and serves later in the operation as a guide for a retention catheter. Each limb of the  $\Delta$  is made to terminate close to the tuberosity of the ischium. A flap composed of skin and fascia is dissected up, and the bulbocavernosus muscles are separated from each other, beginning at the apex of the triangle and working downward. The author states that this separation from the corpus spongiosum as far down as the superficial transverse perineal muscles is easy, but that it cannot be carried beyond the point where these muscles meet the corpus spongiosum. To secure further separation, a hemostat is placed on either side, close to the point where

<sup>38</sup> Journal of the American Medical Association, January 10, 1920.

they join the corpus spongiosum, and they then are divided in such a manner as to leave a portion attached to the latter structure. Two spaces now appear, one on each side of the operative field, between the

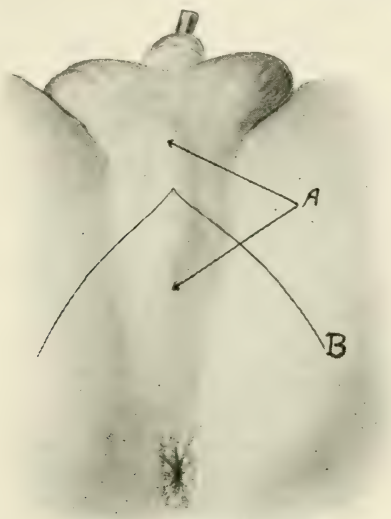


FIG. 26.—A, bulging caused by staff in urethra, the lower arrow corresponding to beak of staff at stricture; B, inverted V incision, its apex well above stricture.

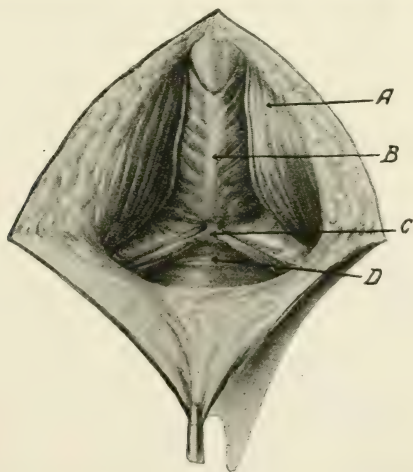


FIG. 27.—Skin flap turned down, exposing structures overlying corpus spongiosum: A, ischio cavernosus muscle; B, bulbo cavernosus muscle; C, junction of the superficial transversus peronei and bulbo cavernosus muscles on corpus spongiosum; D, levator ani muscle.

corpus spongiosum and the corpora cavernosa. Into these spaces the finger can readily be inserted and carried up to the superficial layer of the triangular ligament. With the aid of scissors, the corpus spongiosum is

now freed from the ligament and also from the urethra. This separation can be carried as far as is necessary to give a good exposure of the stricture and the parts immediately above and below it. The urethra

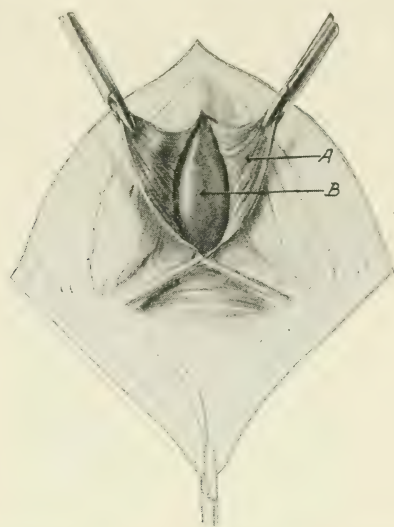


FIG. 28.—*A*, bulbocavernosus muscles separated and held apart, permitting corpus spongiosum (*B*) to protrude.

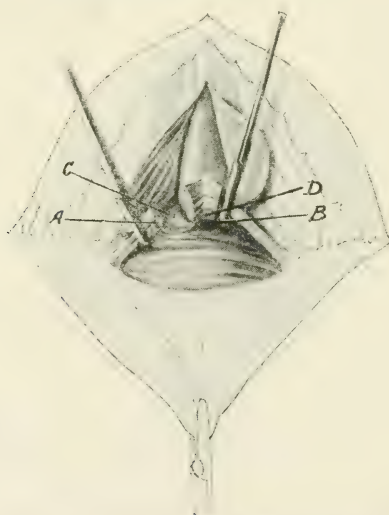


FIG. 29.—*B*, clamps grasping junction of bulbocavernosus and superficial transverse perineal muscles near their attachment to corpus spongiosum; *A*, right side, severe, exposing *C*, superficial layer of the triangular ligament; *D*, muscle stump remaining attached to corpus spongiosum.

is now seized with two Allis tissue forceps, one of which is placed above and the other close below the stricture, and a straight incision then opens the urethra between them. The margins of the incised urethra



are now caught with two more Allis forceps, and two lateral flaps, containing the strictured urethral floor, are removed. This leaves an ovoid opening in the urethra, into which a rubber catheter is inserted, the

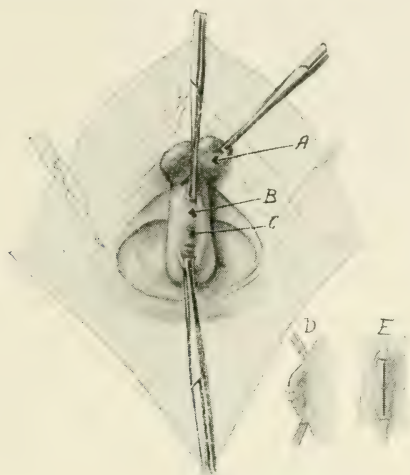


FIG. 30.—*A*, corpus spongiosum elevated exposing urethra; *B*, beak of staff engaged in stricture in urethra throwing it into folds, *C*; *D*, same, lateral view; *E*, Allis clamps placed above and below stricture and line of incision.

filiform now being removed. The open end of the catheter is slipped over the beak of the staff and pulled out through the external meatus.

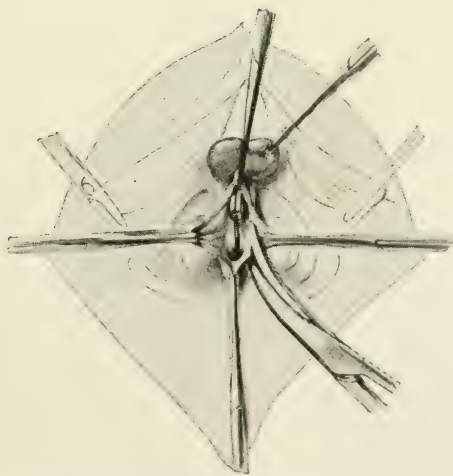


FIG. 31.—Urethra opened; staff and filiform exposed; left stricture bearing flap being removed.

The wound in the urethra is then closed in a transverse direction. The corpus spongiosum is attached to the superficial layer of the triangular ligament by two fine catgut sutures, and the divided ends of the bulbo-

cavernosus muscles are united with the transverse perinei muscle by a single suture passed through both structures from one side to the other. It is also made to include the levator ani muscle. When this suture is tied, the structures are brought into close apposition. Finally, the skin flap is sewed into place with interrupted sutures of silk or linen. At the expiration of forty-eight hours, the catheter is removed and an irrigation given. Then another sterile catheter is inserted and kept in for twenty-four hours. On the next day it is taken out and the patient is catheterized every four hours. On the fifth day he is allowed to void. On the tenth day a 24 F. sound is passed, and a week later a larger one is used. The author states that he does not consider further instrumentation necessary. Immediately after the operation, he covers the operative field with an ointment composed of paraffin wax and vaseline, which acts as a protective dressing and, he thinks, guards against infection.

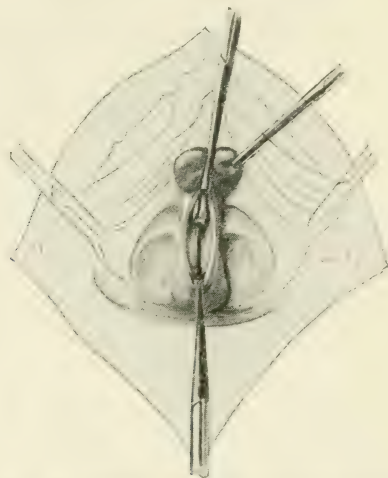


FIG. 32.—Same as Fig. 25; aperture in urethra after removal of stricture tissue may be seen.

This operation, which is undoubtedly ingenious, requires accurate anatomical knowledge and a perineum which has not been converted into a homogeneous fibrous mass. It differs from other resection operations in that care is taken to free the corpus spongiosum from surrounding parts and to guard it against injury. Up to the present time, resection, either partial or complete, has not met with great favor. External urethrotomy, while not curative, assures relief; and if the patient will attend to himself properly afterward, his urethra can be kept patent.

Livermore<sup>39</sup> describes a method of performing external urethrotomy without a guide which has proved very satisfactory in his service at the Memphis General Hospital where many cases of impassable stricture, especially in the negro, are treated each year. In many of these patients the bulbous and membranous portion of the urethra are buried in the

<sup>39</sup> Urological and Cutaneous Review, May, 1920.

cicatricial tissue. The perineum is converted into a fibrous, gristly mass, which is frequently traversed by fistulous tracts. During the first stages of the operation the technic which Livermore uses is that employed by other surgeons. With the patient in the lithotomy position, an incision is made in the mid-line of the perineum over the tip of a sound previously passed down to the stricture. Through this incision the urethra is opened, behind the bulb if possible, so as to lessen hemorrhage. A suture is then passed through each margin of the urethral wound and clamped with a hemostat. Traction on these sutures makes a diamond-shaped opening, which exposes the tip of the sound resting against the face of the stricture. The sound is removed and instead of searching for the opening in the stricture, as is usually done, with the finger as a guide the point of a scalpel is placed directly against the face of the stricture and an incision made through it. The tip of the index finger is then placed in this incision, and by gentle pressure and rotation is made to pass on through the strictured tissues into the urethral opening and thence into the bladder. Sounds are now passed from the external meatus to the bladder, and a large rubber drainage tube,  $\frac{3}{8}$  inch in diameter, with a round end and a hole in each side, is passed through the perineal wound into the bladder. It is held in place by two silk-worm-gut sutures, which also pass through the superficial tissues of the perineum. Gauze is packed around the tube and superficial dressings and the T binder is finally applied. In cases complicated by fistulæ a fine probe or a filiform is insinuated through one of the fistulous tracts and carried on into the urethra. By palpating the perineum, the operator can feel the tip of the probe in the urethra behind the face of the stricture. After both have been located, the scar tissue is incised and the operation completed in the manner above described. All fistulous tracts and abscesses are opened, curetted and drained.

S. H. Harris<sup>40</sup> reports 3 cases of resection of the urethra and describes a method somewhat resembling Stern's plastic procedure. It is based upon principles set forth by Russell, of Melbourne, a number of years ago; namely, that the perineal portion of the urethra may be slit up on its floor to any desired extent; and that any damaged portion may be resected, the ends sewn together and, provided that urinary contamination of the wound be prevented, the urethra will gradually assume its tubular form. The author believes that the practice of these principles will obviate the necessity for the use of sounds after operation. He points out that it is applicable only to those impassable strictures in the region of the bulb, and also lays stress upon the importance of draining the urine by a suprapubic cystotomy, which is performed as a preliminary operation. Resection of the stricture should not be done for at least seven days after the cystotomy. After resection no instruments should be passed through the urethra for at least three weeks and preferably longer. A full size sound is tried first, but if it will not pass easily, smaller instruments are used.

<sup>40</sup> Medical Journal of Australia, January 31, 1920.



Stern,<sup>41</sup> in a paper replete with valuable suggestions, also discusses the *palliative treatment of stricture*. It has been his experience that many patients who go on to an attack of complete retention, do so because of the barbarous treatment to which they have been subjected earlier in the evolution of their urinary difficulty. Many of his patients state that the treatment they received caused so much pain, bleeding and more difficulty in voiding, that they thought they were better off without it. That the utmost gentleness should be used in dealing with these inflamed infiltrates which precede tight stricture is a rule upon which too great insistence cannot be placed. In dealing with them one should always make haste slowly and as Stern appropriately states, it should be borne in mind that inflammation and edema engrafted upon the stricture rather than the stricture itself, are the conditions first to be combated. The old treatment, consisting of a prolonged hot bath and a hypodermic of morphine and atropine, will sometimes enable a patient to void spontaneously. When supplemented by a urethral injection of weak adrenalin and cocaine, immediately followed by another injection of warm sterile oil, an instrument of good size will often readily pass into the bladder without causing the patient pain.

The difficulty encountered in catheterizing patients of this class is often due to the use of instruments of too small a caliber, especially filiforms, the tips of which become caught or imbedded in the inflamed tissues around the stricture. For many years I have successfully used silk-web, olive pointed catheters in these cases, always making an attempt, however, with a firmer and larger instrument before resorting to the former. Stern recommends the ureteral catheter in difficult cases. He also calls attention to the feasibility of getting a very small instrument through the stricture under direct guidance of the eye, passing it through a specially constructed urethroscope which he has devised for this purpose. This method is well known to genito-urinary surgeons. It was successfully used in Philadelphia a decade ago by Schwartz and Dorrance, the former, if I remember correctly, using the old-fashioned Marks air dilating scope. Stern's instrument, which is used with water irrigation, and is of the type of the Geringer instrument, is very ingenious, having a special cannula or instrument channel, which together with the telescope and light carrier, fits accurately into the sheath by means of a water-tight sleeve, thereby permitting forward or backward focussing of the scope without permitting the escape of any water. Stern rightly considers this class of patients as hospital cases and warns against prolonged instrumentation in the office. A number of cases are reported in which the bladder was drained suprapubically. The results were most gratifying, as none of the patients so treated required any further cutting operations. After they had rested in the hospital about ten days and the bladder had drained, it was possible to penetrate the stricture with an instillation tube and later to pass sounds.

**Urethrectal Fistula.** False passages connecting the posterior urethra and the rectum constitute a very serious lesion, not only because of

<sup>41</sup> New York Medical Journal, January 3, 1920.

the abnormal communication which they establish between the two parts, but also because they are almost without exception accompanied by lesions of the deep urethra and the sphincter ani. The involvement of the sphincter ani is of such a nature as to cause permanent incontinence and, in the course of time, to produce sufficient contraction to necessitate dilatation. Fistulae of the urethra likewise are followed by traumatic stricture. These resultant morbid changes are really of more importance than the fistula itself, for the latter will sometimes undergo spontaneous closure.

Recently Velidjani<sup>42</sup> has reported 10 cases, all following war-wounds, which came under his observation in Legueu's service at l'Hôpital Necker, in Paris.

With regard to treatment, he states that the first thing to be done is to drain the urine away from the injured parts through a suprapubic vesical opening. If the urethra is permeable, a retention catheter is used, it having been found that the fistula closes more readily under this treatment. In all cases the caliber of the urethra must be restored, whether it be permeable to a small retention sound at the beginning of treatment, or whether a stricture of small caliber has already been formed. Progressive dilatation should be practised at regular intervals, beginning with as large an instrument as can readily be passed. In cases in which an impermeable stricture is encountered, external urethrotomy should be performed; and when this operation is necessary, attention should be given to the fistula at the same time, an attempt being made to dissect the urethra away from the rectum. Closure of the openings by suture may be attempted, if desired; but if a complete separation can be made of the urethra from the bowel, the author believes that the break in continuity of each structure will probably be as well repaired by nature. In those cases in which the fistula is not very large, and in which the stricture proves amenable to dilatation, either by the retention catheter or by the use of sounds at intervals, the author advises against too early operative interference, experience having shown that the fistula has a tendency to close.

**Gonorrhea.** Not many references to *acriflavine* appear in the year's literature; and those authors who have reported their experiences do not, for the most part, seem enthusiastic. Birchfield<sup>43</sup> is of the opinion that the average duration of treatment is less than with the older methods. Harrison<sup>44</sup> states that the effect is not magical, and that the discharge quickly returns if the irrigations are left off too soon after it has ceased. This ought not to be an indictment of the drug, however, as the same thing applies to the older remedies. The most recent article that I have seen is one by Hyman,<sup>45</sup> of New York, who summarizes his experiences with *acriflavine* in 52 cases treated by the injection method. His results have been very encouraging. In his series there were 20 cases of acute anterior urethritis, 12 of acute posterior urethritis, 10 of

<sup>42</sup> Arch. Urolog. de Necker, 1919, vol. ii.

<sup>43</sup> United States Naval Medical Bulletin, October, 1919.

<sup>44</sup> Venereal Diseases in General Practice, 1919.

<sup>45</sup> Urologic and Cutaneous Review, June, 1920.

subacute and chronic urethritis, and 13 associated with prostatitis, vesiculitis and epididymitis.

In two of the acute anterior cases, it is stated that a cure was obtained in four days; in 3, in six days; in 4, in nine days; and in 2, in two weeks. The remaining 9 cases, however, did not respond with such readiness. In 4, the infection spread to the posterior urethra; and in 3, relapses took place within forty-eight hours after apparent cure. After using the drug for periods varying from five to seven weeks, apparently without any improvement, the treatment was discontinued. In 5 of these cases, examination showed that the gonococci had become embedded in the follicles and in the deeper layers of the urethral mucosa. The results obtained in the 12 cases in which the posterior urethra was involved were not so satisfactory. In fact, the author states that they were no better than those which follow treatment with other remedies. The average duration of treatment in these cases before a cure was brought about was forty-three days. The question naturally arises whether slight recurrences may not have taken place in some of the more favorable cases, just as they do in cases treated with other remedies, the patients either ignoring them or seeking treatment at other places. In the subacute and chronic anterior group examination showed that all the patients had folliculitis and various degrees of submucous infiltration. Two of the patients thus affected were apparently cured in three weeks with flavine injections. The remaining five required from four to seven weeks of dilatation in addition to the injections. The patients in the remaining group required treatment for their complications, so that the injections were used only as an adjunct to the principal measures employed.

Hyman mentions 10 additional cases in which he has resorted to irrigations with a 1 : 4000 solution, according to the method of David Watson, which was discussed in this review last year. He expresses the opinion that they are of greater value than injections of the stronger solution. He states that the discharge, no matter how profuse it may be, disappears or becomes very scanty by the end of the first week's treatment. Finally, he expresses the opinion that acriflavine in strengths of 1 : 6000 to 1 : 4000 in normal salt solution is the best antiseptic that we possess for irrigations in the treatment of gonorrheal urethritis.

E. G. Davis<sup>46</sup> has made another report, based upon a series of 34 cases, in all of which the disease was limited to the anterior urethra. The patients received two injections daily of a 1 to 1000 solution, each injection being retained five minutes. The secretion was examined daily for gonococci. The time at which treatment was begun varied from the first to the thirtieth day after the onset of the discharge. No constant relationship between duration of infection and response to treatment was noticed, with the exception that brilliant results were obtained in some of the cases in which the treatment was begun very early. The most persistent infections, however, were not those of particularly long duration. In some cases of two or three weeks' dura-

<sup>46</sup> Nebraska State Medical Journal, January, 1920.



tion the symptoms yielded promptly. Treatment was not continued in any case longer than twenty-one days, and those cases in which gonococci had not disappeared from the discharge and the patient had become free from symptoms at the expiration of that time were considered as failures. In 16 out of the 34 cases an apparent cure was obtained. There were 9 cases, however, in which the drug was apparently without effect and 9 others in which the results were very indifferent. In five of the failures the gonococci persisted in the discharge, whereas in the remaining four they would disappear for a short period only to reappear again. There were 9 cases which the author terms the indifferent ones, in which the gonococci disappeared promptly and could not subsequently be found, but in which a slight discharge kept up. In discussing the 16 cases apparently cured, Davis states that the average period during which the patients were kept under observation was twenty-five days and that the average duration of treatment was nine days. Thus it would seem that they were free from symptoms only sixteen days. As in Hyman's series, the question naturally arises whether recurrences may not have taken place after the patients passed from observation. However, the circumstances of the disappearance of gonococci from the discharge within a few days after the beginning of treatment, the subsidence of the discharge itself and the absence of symptoms for a period exceeding two weeks, all speak in favor of the efficacy of the drug. While making no extravagant claims for this drug, Davis believes that it is superior to the various organic silver preparations. In the author's paper the results of further laboratory studies are also published.

My own experience with acriflavine and proflavine has not been satisfactory. Of the two, acriflavine seems to be the more efficacious in the sense that it quickly suppresses the discharge. Patients upon whom I have used it have been greatly pleased with its primary effects and, likewise, greatly disappointed when a gonococcus-laden discharge has come back after the cessation of treatment. In a few cases chronic discharges have apparently been cured by its use.

Another new drug, also a dye, has been recommended since the publication of last year's review, namely: *Mercurochrome 220 soluble*, which is the di-sodium salt of di-brom-oxymercury fluorescein. Young, White and Schwartz,<sup>47</sup> of the Brady Urological Institute, consider it of value in all urethral infections except hyperacute cases of gonorrhea, in which it has been found too irritating. Combining as it does 25 per cent. of mercury in organic form with fluorescein, it exercises the double action of a germicide and a penetrating dye. With regard to the latter the readers of this review may remember that attention was called some years ago to the use of a solution of fluorescein in the treatment of genital and urinary infections. *Mercurochrome* does not produce the chemical reaction of other mercury salts and it does not precipitate protein; consequently it is not decomposed by urine, and can be applied to mucous surfaces without producing the same degree of

<sup>47</sup> Journal of the American Medical Association, November 15, 1919.

irritation that the ordinary mercury compounds produce. It is usually employed in a 1 per cent. solution, although the authors state that it may be used as strong as  $2\frac{1}{2}$  per cent. It should be preceded by an injection or irrigation of warm sterile water or normal saline solution. For anterior urethritis a dram or two should be injected and retained in the urethra for five minutes. The authors state that it may be used as often as every three or four hours. In posterior urethritis one-half to one ounce may be injected, either through a catheter or by means of the posterior urethral syringe. As soon as the discharge has become free from gonococci, the injections should be reduced in frequency, and entirely discontinued at the end of a week. For the mucoid discharge which sometimes follows this treatment, irrigations of weak potassium permanganate, or nitrate of silver solution 1 to 10,000, are recommended. In this connection it is important to remember that potassium permanganate should not be used in conjunction with the mercurochrome either as a preliminary irrigation or as additional treatment.

The narration of some experiments carried on by the authors to determine the penetrating power of this drug may prove interesting. Rabbits were catheterized with a small soft rubber catheter through which an ounce of a 1 per cent. solution was injected after the urine had been withdrawn. The catheter was removed very slowly, so that some of the fluid might escape into the urethra. Five minutes later the bladder was emptied by the catheter, the rabbit killed and the bladder and urethra removed. Then the bladder was opened and the excess of the solution washed out with water. Frozen sections of bladder and urethra were at once made and showed that the epithelial cells of the urethra were stained deep red. This staining was deepest in the superficial layers and diminished in intensity as the submucosa was approached; certain areas of the latter, however, were stained and in some spots the dye had reached the muscularis. The bladder epithelium was similarly stained, but the dye did not penetrate so readily to the submucosa as it did in the urethra. This experiment was performed on several animals, and in some cases, under general anesthesia, the abdomen was opened and the ureter exposed and injected. The renal pelvis was also injected in certain cases and upon postmortem examination it was found that some of the dye had been taken up by the cells of the collecting tubules as well as by the epithelium in the kidney pelvis itself.

My own experience with mercurochrome has not been extensive, but at the present time I am inclined to believe that it will prove a valuable addendum to the therapeutic armamentarium of the genito-urinary surgeon. A number of rebellious cases of gonorrhea, characterized by recurrence after discontinuance of treatment, have yielded to its use. In some cases, when perhaps it was continued too long after gonococci had disappeared from the secretions, it caused a profuse mucoid discharge. The same thing was noticed in cases in which patients were directed to begin a second course of treatment with it after having used a mild astringent or potassium permanganate following the first course of treatment. This was done solely as an experiment to observe what effect it would have. I have not used any solution stronger than 1 per



cent. and in a few cases have found that patients could not inject it more than twice a day. The great objection to it on the part of patients is the one common to all dystuffs: that it stains everything with which it comes in contact—skin, raiment, utensils, toilets and bath tubs. These stains can be removed by a 2 per cent. solution of potassium permanganate followed by a 5 per cent. solution of oxalic acid. On the whole I am more impressed with mercurochrome than with flavine.

The authors also recommend its use in case of pyelitis, in which it is injected through the ureteral catheter. They have likewise found it valuable in chancroids and other non-syphilitic ulcerations of the external genitals. For the latter it may be applied in solution on pledgets of cotton, as a starch paste, or in the form of lanolin ointment. The aqueous solution, however, has been found to be better than the paste or ointment.

A new preparation of an old drug, named *iodargol*, which is a colloidal iodine, has been used with success by Beyler and Duroeux.<sup>48</sup> In early cases, the urethra is first washed out with a solution of permanganate, 1 to 10,000, after which 3 c.c. of iodargol is injected into the anterior urethra and retained for five minutes by compressing the end of the penis. When the entire urethra has become involved, a urethrovesical irrigation with the weak permanganate solution is given; and then, after the patient has completely emptied his bladder, 2 c.c. of iodargol is deposited in the deep urethra by means of a small instillating syringe. No trouble has ever followed this procedure, the iodargol apparently being without any irritating properties. Patients so treated have stated that they experienced relief after the first instillation. The discharge, however, is considerably increased but it begins to diminish after the third or fourth treatment. Microscopic examination during the stage of increased discharge shows a preponderance of leukocytes, an increase of extracellular gonococci, and a decrease of intracellular organisms. In one chronic case in which no specific microorganisms had been found in the discharge, a single instillation of iodargol caused them to reappear. In conclusion, Duroeux states that he considers this preparation superior to any that he has previously used.

Castellani,<sup>49</sup> having found that bile and bile salts prevent the growth of the gonococcus, tried a solution of *taurocholate of sodium in glycerin* as a prophylactic against gonorrheal infection. Two experiments were made on the human subject; in the first instance gonorrheal pus mixed with the solution for three minutes was injected into the urethra. In the second the solution was applied first, then the gonorrheal pus after an interval of three minutes. The subject then urinated and injected more of the taurocholate solution. In neither case did infection occur.

The author states that this solution is not irritating as are some of the silver salts used for prophylaxis and that it is also cheaper. For practical purposes the instillation of a few drops into the anterior urethra before

<sup>48</sup> Concours médicale, November 2, 1919.

<sup>49</sup> Presse médicale, February 14, 1920.



coitus and also afterward are recommended, the second instillation being made after the parts have been thoroughly cleansed with soap and water.

E. F. Müller,<sup>50</sup> of Hamburg, reports his experience with provocative injections of a lactalbumin known as *aolan* in a series of cases in the Marine Hospital, and compares them with the results obtained from similar provocative injections of specific substances, such as vaccine and blood serum. In using *aolan*, the object is not to immunize the individual against lactalbumin, but to produce a high degree of irritation, so that the protective powers of the system may be increased. Two subdermal injections of 0.2–0.3 c.c. of *aolan* are administered on the flexor surface of the forearm. Care must be taken not to give the injection beneath the true skin. The author speaks of these injections as intracutaneous, rather than subcutaneous. A leukocytosis rapidly follows the injection of this substance, but it does not afford a means of differentiating between cases of cured and of uncured gonorrhea. In about six hours after the injection, however, a slight itching is felt in the urethra. This is followed by a considerable increase of urethral secretion, which, as a rule, is accompanied by the appearance of a great many pus cells. Examination of this secretion shortly after it appears or during the following day will show the presence of the gonococcus in cases in which that organism has not become extinct. At least, this is the opinion that Müller expresses as the result of more than fifteen hundred cases in which he has used the method. It proved successful in cases in which the usual provocative methods had failed. There were some cases of one, or even two years' duration, in which only a slight intermittent mucoid discharge had been present, but in which the gonococcus was demonstrated after the *aolan* injections had been given. In conclusion, the author states that he prefers these to vaccine injections, as well as to local irritating methods, such as injections of silver nitrate.

In this connection it may be of interest briefly to discuss PROTEIN or NON-SPECIFIC methods of treatment. From the time that vaccine and serum therapy were introduced some doubt existed as to whether the effects following the administration of these substances did not depend in part, at least, upon certain non-specific proteins or albuminoids contained in them. More than twenty-five years ago Fränkel proposed the use of a heterogeneous vaccine in typhoid fever. Shortly thereafter Hallopeau and Roger treated lupus vulgaris with vaccines prepared from cultures of the streptococcus and the *Bacillus prodigiosus*. Still later Renaud employed antityphoid vaccines apparently with good results in the treatment of certain affections which etiologically had nothing in common with typhoid fever. It is well known that antimeningococcus serum has been extensively used in the treatment of gonorrheal arthritis and other complications of gonorrhea. The late William J. Roe obtained startling results at the Philadelphia Hospital by administering massive doses of diphtheria antitoxin in cases of cancerum oris. It is especially within the last three years, since the

<sup>50</sup> München. med. Wehnschr., January 2, 1920.

investigations of Schmidt and Kaznelson have been reported to the profession, that further attempts to apply proteins therapeutically have been made. In 1915, Schmidt suggested that injections of milk would prove just as efficacious as those of peptone, deutero-albumose and normal horse serum. In Germany such injections have been employed in a variety of diseases, including tuberculosis, progressive anemia, malaria and acute articular rheumatism. In the treatment of venereal diseases also a number of experiments have been carried out. The consensus of opinion seems to be that the extra-urethral complications of gonorrhea are the ones which are the most susceptible to this form of therapy.

The most recent article dealing with this subject which has come to my attention is one by Trossarello,<sup>51</sup> an assistant in the University Clinic in Turin. He has treated 45 cases of gonorrhea with intramuscular injections of milk given in the usual way in the buttocks. In this series there were 8 cases of acute urethritis, 2 of urethrocystitis, 3 of prostatitis, 10 of epididymitis, 2 of arthritis and 20 of salpingitis. The milk used was either sterilized and put into air-tight vials or was boiled extemporaneously and injected as soon as it became sufficiently cold. The initial dose was 5 c.c. which was progressively increased to 10 c.c. In the majority of cases the injections were very well borne. In a considerable number of patients a slight local reaction occurred at the site of injection, but it lasted only a few hours. The constitutional reaction, however, was severe, the temperature rising rapidly to 37, 39 or even 40° C. It was accompanied by headache, general malaise and exacerbation of pain at the site of the local lesions. These phenomena were followed in seven or eight hours by profuse sweating. The symptoms were most pronounced in those who already had some elevation of temperature, being milder in those who had subacute or chronic complications. Five injections were given at intervals of three or four days.

In summarizing the therapeutic results obtained in this series of cases the author states that while they may be considered negative in cases of urethritis and urethrocystitis and uncertain in cases of prostatitis, epididymitis and arthritis they were certainly beneficial in cases of salpingitis and pyosalpinx. The results obtained in the latter class were far superior to those which the author has observed following injections of vaccines and sera. In every case there was a rapid cessation of pain, which in many cases completely disappeared. The author also discusses the manner in which the systemic reaction as well as the therapeutic action is brought about, but as the theories advanced are of a purely scientific rather than of a practical nature, that aspect of the method will not be entered into here.

At the last meeting of the Italian Society of Dermatology and Syphilography one of the subjects exhaustively discussed was *serum and vaccine therapy of gonorrhea*. The reporter, Morini,<sup>52</sup> after reviewing the subject from every standpoint summarized his conclusions, which, I think, may be accepted as representing the present status of this method of therapy.

<sup>51</sup> La Riforma Medica, April, 1920.

<sup>52</sup> Giornale Italiano delle Malattie Veneree e della Pelle, June 3, 1920.

With regard to serum therapy, the reporter states that the consensus of opinion of a large number of observers is to the effect that the serum exerts no action whatever upon the primary localizations of the infection, such as acute urethritis in the male, vulvovaginitis in female infants or children, and endocervicitis and urethritis in the adult female. It has an appreciable, although not a constant effect, in epididymitis and a slight action in other regional complications such as Cowperitis, prostatitis and Bartholinitis. In salpingitis it seems to exert a fairly constant action, at least upon the systemic phenomena accompanying involvement of the adnexa. In septicemia it reaches its highest degree of efficacy, the results often being brilliant.

The author, however, calls attention to the fact previously referred to above that similar results have been obtained in the same complications by the injection of other sera. He also points out that in the cases in which no marked clinical improvement follows the injection the defensive elements of the organism are probably increased by the action of the serum.

With regard to vaccine therapy a greater diversity of opinion was found to exist. He feels that it is permissible to express the opinion that the action of vaccines upon the regional and hematogenous complications of the disease are generally good, although they are by no means constant. In the reports which he obtained the most varied opinions were expressed. The consensus of opinion was that they had no action whatever upon acute, subacute or chronic urethritis, although a few authors reported some success with them. The same thing applies to vulvovaginitis. The absence of acquired immunity, the apparent existence of a special predisposition to reinfection or superinfection, and the liability to regional or hematogenous metastases are all conditions which seem to show that in the cure of gonorrhea the phenomena of immunity play a very small part. Therefore it is not surprising that serum and vaccine therapy has not been universally successful in the treatment of this disease and its complications. In this review some years ago my own experience with these substances was summarized. Time has not served to change the opinions then expressed. The vaccines I consider valueless. The serum has proved beneficial in certain systemic phenomena accompanying the development of lesions in proximal or remote parts of the body. I still use it in acute arthritis and also in prostatitis associated with severe febrile reaction. Since I have been operating on my cases of acute epididymitis, I have had no occasion to give serum injections. I am well aware that there are a few authors who claim a high degree of efficacy for the vaccines. Their experience has been entirely different from my own.

Reasoning by analogy from the methods which have proved so successful in the treatment of cerebrospinal meningitis, Debré and Paraf<sup>53</sup> undertook the treatment of GONORRHEAL ARTHRITIS by injecting the serum directly into the affected joints. Before resorting to this form of therapy, however, they conducted some experiments upon

<sup>53</sup> Bulletin et mém. de l'Soc. méd. d. hôp. de Paris, November 6, 1919,



rabbits, injecting the gonococcus directly into the anterior chamber of the eye, and then following the injection twenty-four hours later with an intra-ocular injection of antigenococcus serum. The lesions produced by the endotoxins of the injected microorganisms were materially modified by the subsequent injection of serum; and the authors were so encouraged that they determined to apply the treatment to gonorrheal arthritis in man.

Fifteen cases are reported, in all of which the joint lesions were of recent origin. All were characterized by severe pain, large effusions, elevation of temperature and disturbance of general health. Left untreated, the authors believe that all of these cases, after many weeks of continued fever and pain, would probably have resulted in ankylosis of the diseased joints. In fourteen of the number the results were favorable; in six, a cure was obtained in less than a week; and in the remaining eight, in less than two weeks. The term cure is used in the sense that the local symptoms had disappeared and the joints had recovered their power of function. In one case the treatment was a complete failure, the patient being a pregnant woman in very bad general condition who died a few days after she had been delivered.

The technic of the treatment is simple: The joint is aspirated and a quantity of serum slightly less than that of the fluid drawn off is immediately injected into it. A firm dressing is applied. It is necessary to repeat the treatment two or three times, either every day or every second or third day. For example, in 6 cases, two injections were given; in 4, three injections; in 3, four injections; and in 2, five injections. There were 6 cases of multiple arthritis involving two, and even three, joints. In these, all the joints were injected at the same seance. In 5 cases, intramuscular injections of the serum were also given; and in 3 cases, intravenous injections. While the authors believe that in these conditions the injections so given exert no action upon the affected joints, they administered them with the hope of influencing the general condition of the patient and preventing the development of fresh localizations of the gonococcus. In 4 cases, there was a sharp local reaction, associated with increased fever. It lasted only a few hours. Debré and Paraf believe that the most serious objection to the method consists in the circumstance that small joints are so frequently involved. These, of course, cannot easily be aspirated and injected. For inflammation of the larger joints, especially the knee, they think that the method will give gratifying results, provided that it is used soon after the joints have become involved. The question of preparing different serums against different strains of gonococci, as is done in the case of the meningococcus, was considered. At the time their paper was published, however, the authors had not been able to make a differentiation of the microorganisms that would warrant an attempt to prepare such a specific serum.



# SURGERY OF THE EXTREMITIES, SHOCK, ANESTHESIA, INFECTIONS, FRACTURES, DISLOCATIONS AND TUMORS.

By WALTER ESTELL LEE, M.D.

THE two years which have intervened since the return of the civilian surgeons from their military experiences have provided sufficient time to show an effect upon civil surgery. Of course, this period really has been one of six years and though in last year's review we were cautious in our statements as to the permanency of the contributions from this military experience, it is gratifying to see that the literature of the last twelve months requires little change in the statements we then made.

The men as they have returned to their civil practices have first reported their personal experiences and later the application of them to the problems in their civil practice.

In the treatment of *traumatic wounds* in military surgery one still reads almost universally favorable reports of the newer methods. Bowlby<sup>1</sup> says that the use of antiseptics in grossly contaminated tissues without débridement or mechanical cleansing have all proved valueless. Primary or delayed primary suture of infected traumatic wounds should always be the objectives. Wounds containing a considerable number of micro-organisms will heal, provided they do not include virulent streptococci. This really summarizes, in a concrete way, the lessons learned from the massive traumatic war wounds. Their greatest application in civil practice, of course, is in industrial wounds, but the percentage is small compared to those encountered in military hospitals, and one finds these returned military surgeons experiencing difficulty in making themselves and their assistants as conscientious and painstaking in the care of infected wounds as they were in the Army. This comment is not an excuse but a criticism. In the Army, where efficiency was the standard by which all treatment was measured, surgeons were compelled to give to traumatic wounds maximum care, and the results obtained have established new standards. In civil life, not only is this group of traumatic wounds a very small proportion of the surgeons' problems but, as yet, the patient, the employer and the community have to be educated to the possibilities of maximum surgical treatment and to appreciate that such treatment, though very much more expensive at the time being, is by far and away the cheapest in the end.

Babcock<sup>2</sup> complains, "A treatment successful in the hands of highly skilled enthusiasts may fail in routine use when it exacts infinite care

<sup>1</sup> Lancet, London, January, 1920.

<sup>2</sup> Journal of the American Medical Association, May 8, 1920, No. 79, vol. lxxiv.



as to detail over prolonged periods of time. The average surgeon is not constituted to stand on tiptoe all the time, his technic is not invariably perfect, and his soul rebels against the constant infliction of pain, and it is therefore not strange that so many surgeons have failed in their Carrel-Dakin treatment of wounds." Such a statement is not borne out by the experience of most surgeons, and, if it were true, we still maintain that, with the definitely improved results it has been possible to obtain by such treatment, no surgeon would be justified in excusing himself instead of trying to master the details of the method until a better treatment is developed.

The treatment of war wounds has revolved around the principles of asepsis and antisepsis, and, though at first antiseptics were largely depended upon, they were found to be entirely inadequate as they have been in civil surgery. The real advance has been in the recognition of the etiological factors of infection. The character of the organism, the streptococcus being a law unto itself and of such virulency that the tissues cannot be depended on to take care of it; the interval of time elapsing between the implantation of the organisms and their surgical removal; the absolute necessity of removing, at the earliest possible moment, dead and devitalized tissues which not only provide culture media for the rapid growth of the infecting organisms, but also prevent access and necessary contact between the vital resisting substances of the normal living tissues, and the organisms; and the earliest possible closure of the wound with a skin covering to prevent subsequent reinfection.

It is generally conceded Bowlby's statement that the use of antiseptics in grossly contaminated wounds, without the removal of the dead tissues, with the knife or mechanical cleansing, have all proven valueless. The single exception is Dakin's solution, and Lee has shown<sup>3</sup> Dakin's solution should not be looked upon as a germicide but as a solvent of dead tissues, because of the hydroxides that are formed when the hypochlorites come in contact with the chemical substances in such tissues. Dakin's solution should be regarded as a chemical method of débridement. This question is reviewed in detail under the subject of Antiseptics. Thus we return to the same position as in the beginning of the War. The best means of treating infected wounds is in the prevention of them by asepsis. That wounds that have become infected should be treated first by removing the etiological factors of infection, bacteria and dead and devitalized tissues. Mechanically, if possible, chemically as a second resort or to supplement mechanical removal. The only way to insure their remaining sterile, after such mechanical or combined mechanical and chemical treatment, is to close them and insure their covering with intact skin.

The prophylactic value of *antitoxin in tetanus* was clinically proven in the War. The clinical reports of the last year entirely confirm this experience. A distinct contribution to the subject is in the publishing of the experimental investigation that was carried on by the British

<sup>3</sup> Lee: *Annals of Surgery*, May, 1920.

Council of Medical Research during the War. This is not only confirmatory of the clinical experience in the prophylactic value of anti-tetanic serum but is also suggestive of lines along which therapeutic results can be obtained.

In the question of *shock*, Bowlby<sup>4</sup> calls attention to the fact that the war experience has shown rough transportation after injuries is as potent a cause of shock as is the original gunshot wound itself. This can be obviated by the early application of suitable splints, and the principle should be employed in all injuries and not confined alone to fractures. This has a distinct practical application in civil surgery, for the Thomas splints, for the upper and the lower extremities, should be a part of the equipment of every first-aid station, every ambulance and patrol wagon and accessible in the receiving ward of every hospital.

Shock and hemorrhage are no more considered as two distinct conditions, requiring differentiation from one another for their proper treatment, but their real relation is that of cause and effect. The group of symptoms called shock can be described as a condition of circulatory failure. This circulatory failure may be brought about by actual loss of blood, as in hemorrhage, or relative loss of blood, as in capillary stasis. The capillary stasis may be the result of nerve exhaustion, as in primary traumatic shock, or a toxic poisoning, as in secondary traumatic shock. Irrespective of the cause, the condition is one of circulatory failure in which there is an actual or relative loss of blood volume and a fall of blood-pressure. To restore these, rest, warmth and the taking of fluids have proven to be of the most value. Normal rest, if possible, but morphin to produce artificial rest if this cannot be obtained because of pain, anxiety and excitement. Fluids should be administered preferably by the mouth or rectum, for when given in this way they are more likely to permanently improve blood-pressure and blood volume than when given intravenously. When shock is due to excessive bleeding, the immediate infusion of blood gives far better results than any artificial solution, not excepting gum acacia or Ringer's solution.

The literature on *anesthetics* is entirely in accord with the statement of Blake<sup>5</sup> quoted last year: "The consensus of opinion is that probably nitrous oxide with oxygen will be employed in the future to the exclusion of other general anesthetics except ether, which will be used as an adjunct." Dale<sup>6</sup> has made a very valuable contribution to the subject of anesthesia in an experimental way. He found that after inducing experimental shock in a series of animals with uniform doses of the chemical histamine, a substance which is similar to, if not actually the same as, the chemical products obtained from dead and devitalized tissues, he was able to demonstrate constantly that the greatest degree of shock would follow the use of chloroform, next ether, and the minimum degree always when nitrous oxide and oxygen were employed.

The necessity for the prompt closure of wounds of the pleural cavity

<sup>4</sup> Lancet, London, January, 1920.

<sup>5</sup> PROGRESSIVE MEDICINE, December, 1919, p. 207

<sup>6</sup> British Journal of Experimental Pathology, April, 1920, i, 103.



was not appreciated during the early part of the War nor until long after this was practiced in wounds of the other tissues. Its practical application in civil surgery has been in the employment of the same principles for the sterilization of infected pleural cavities, as has been so valuable in the treatment of infected wounds in other parts of the body. Drainage, chemical débridement with Dakin's solution, and, after surgical sterility has been obtained, the delayed secondary suture of the wound, has definitely improved the end-results obtained from the surgical treatment of empyema.

In the treatment of *fractures*, Jones<sup>7</sup> feels that the lessons civilian surgeons should learn from war surgery are clear. If such results as Bowlby reports, an average of less than 0.5 cm. of shortening in fractures of the femur during the last year of the War, can be obtained by such simple apparatus as the Thomas splint in compound fractures of war, why should students be taught that fractures of the femur can only be adequately dealt with by plates and screws or other internal splintage. In the treatment of compound fractures, Blake's principle of applying traction to the distal fragments of the bone in the direction of its long axis with the limb in a neutral position (muscular rest), is just as applicable to civil fractures as to war fractures. Bowlby said that the use of extension and suspension methods which provide circulation, and hence nourishment of the tissues and mobility of the limb, should entirely replace the use of plaster of Paris, wooden boxes and constricting bandages. Those surgeons who were interested in fractures before the War have had that interest developed to an even greater extent, and the younger men who were not fixed in their surgical likes and dislikes have developed a new interest in fractures, but the large majority seem to have returned to civil life with the same old attitude of letting the fractures heal themselves and in trusting them to the tender mercies of the house officer and the nurse. Here again, the Army Medical Corps has established high standards. Bowlby's report of less than 0.5 cm. of shortening as the average of the results obtained in the R. A. M. C. during the last year of the War, are quite different from those we had been content with in the past. In the future we should not be content with anything less but until the patient, the employer, or the community demands and is willing to pay directly and indirectly for such results, the average surgeon will probably become discouraged with this type of work.

In the *surgery of the joints*, Gunn<sup>8</sup> feels that one of the greatest contributions of war surgery is the recognition of the fact that the serous membrane of the joint cavity has a surprising capacity for resisting infections. The substitution for mobilization instead of immobilization of joint infections, after the synovial cavity has been opened, is being conscientiously tried in civil practice. Its results in war wounds were unquestionable, but there is little in the literature of the last year that has any bearing on this subject.

<sup>7</sup> Surgery, Gynecology and Obstetrics, January 30, 1920, No. 1, xxx, 7.

<sup>8</sup> Canadian Association Journal, April, 1920.



**Shock.** John Hunter, in 1774, was probably the first to describe shock. For nearly a century investigators and clinicians have been propounding theories and promulgating doctrines that have failed, without exception, to stand the test of searching criticism. The elder Gross described shock "as a rude unhooking of the entire machinery of life." This all-inclusive definition has been accepted up to the present time and is undoubtedly responsible to a certain extent for our present lack of knowledge of the condition.

In last year's review<sup>9</sup> we quoted Cannon's<sup>10</sup> suggestion "that shock be considered as a general body condition in which the central fact is circulatory failure." The literature of this past year has shown a more or less general acceptance of this definition. Whether this circulatory failure be the result of psychic overstimulation and consequent exhaustion, as held by Crile and Lower,<sup>11</sup> or traumatism, sepsis, toxemia, foreign peptone, anesthesia or hemorrhage, the common term shock can thus be applied to the resulting clinical symptoms which are always so much alike. A realization that shock, like so many other phenomena, is the result of a complex interplay of many factors, and that any one of them may initiate a departure from normal which will result in circulatory failure has already been productive of clearer thinking and distinct advances in both research and clinical treatment.

W. M. Bayliss<sup>12</sup> differentiates, from all other forms of shock, the type which is of nervous origin and calls it *primary shock*. He says that it is analogous to fainting, and differs from it only in its greater severity and longer duration. Low blood-pressure is the most important feature of this condition, and, when this pressure is restored, the other symptoms disappear. He groups all other forms as secondary, and adds the most obvious etiological factor to this generic term as *secondary traumatic shock*, *secondary septic shock*, or *secondary surgical shock*. This type is slower in onset, of longer duration and of much greater severity. He speaks of it as a "state of collapse associated with low blood-pressure which results in a deficient circulation of the blood and deprivation of the tissues of their necessary supply of oxygen."

**PRIMARY SHOCK.** It is not surprising that the comparative importance of the different factors concerned in the production of circulatory failure should impress different observers in different ways. Thus, Crile and Lower, in the latest edition of their monograph on *Surgical Shock*,<sup>13</sup> still feel that the condition is always the result of exhaustion of the central nervous system. Seelig<sup>14</sup> suggests that they approach the line of speculative metaphysical reasoning in their attempt to prove that the morphological changes in the ganglion cells are the prime cause of shock. Though their work has been all too scantily confirmed by other investigators, they claim that the cell changes described by them are constant and are so invariably present that there is no doubt

<sup>9</sup> Lee: PROGRESSIVE MEDICINE, December, 1919, p. 208.

<sup>10</sup> Journal of the American Medical Association, July, 1919, lxxiii, 177.

<sup>11</sup> Surgical Shock, Saunders & Co., 1920.

<sup>12</sup> Proceedings of the Royal Society of Medicine, London.

<sup>13</sup> William B. Saunders Company, 1920.

<sup>14</sup> International Medical and Surgical Survey, April, 1920.

of their significance. Unfortunately, no one up to the present time has brought forth complete data in rebuttal of their work, and the statement that the histological changes in the brain cells in shock and exhaustion, from any cause, are always identical, cannot be controverted. But the fact that these cell changes in the central nervous system are always present in shock does not prove that they are the primary cause of it. Crile and Lower demonstrate that brain-cell changes, exactly similar to those produced by trauma, are seen in fear, senility and numerous other states, and thus link together a group of many causes while striving to prove that the etiological factor underlying shock is a definite symptom-complex. Not only do changes in the nerve cells follow insult from the various etiological factors concerned in shock, but also changes in the cells of other tissues and the results of these cell changes vary according to the functions of the cells involved. Thus, in secondary septic shock, the nerve cells probably are the last to be involved, while in primary traumatic shock the nerve changes are of primary importance.

Crile and Lower, in their enthusiasm for their theory of shock, have failed to develop the necessary research into the disarranged functions of body tissues other than the nerves. It would seem as though they had a blind side to their vision of the problem. But this much is certain—whatever the theoretical significance of brain-cell changes in shock may be, the practical significance of the theory, as developed by them, is colossal in its imperative emphasis on the necessary qualifications of an operating surgeon—thoughtfulness, deliberateness, gentleness and dexterity.

As Crile and Lower have ventured to rewrite and augment their former monograph because of "their accumulated experience in the civilian clinic and the base hospitals in France," it is only just to quote at length from this new edition.

Though there is little change in their presentation of their Kinetic Theory of Surgical Shock, we quote it in detail. When a barefoot boy steps on a sharp stone there is an immediate discharge of nervous energy in his effort to escape from injury. This is not a voluntary act. It is not due to his own personal experience (his ontogeny), but is the result of the experience of his progenitors during the vast periods of time required for the evolution of his species (his phylogeny). The wounding stone made an impression upon the nerve receptors in the foot similar to innumerable injuries, as a result of which this nerve mechanism itself was evolved during the boy's vast phylogenetic or ancestral experience. The stone supplied the phylogenetic association, and the required discharge of nervous energy automatically follows.

In like manner, all actions are performed. Every adequate stimulus awakens an ontogenetic or phylogenetic memory or *association*, and the nerve mechanism evolved by countless similar experiences in the life of the individual, or of his race, makes the adequate response. These *associations*, like that awakened by the sharp stone in our illustration, may be injurious to the individual—*nocci-associations*; or they may be of benefit to the individual—*bene-associations*. The sight of



appetizing food is a *bene-association*; it awakens both the phylogenetic and the ontogenetic memory of similar experiences. The nerve centers are stimulated as if the food were being actually eaten, and the "mouth waters."

All of life, therefore, is made up of *bene-* and *noci-associations*, and the constant effort of the individual and of the race is to increase the former and decrease the latter; to develop an environment which shall, as far as possible, be free from *noci-associations*—to reach a state of *anoci-association*.

Man is constantly beset by *noci-associations*, such as cold, rain, pathogenic bacteria, and is as constantly striving to reach a state of *anoci-association*. An umbrella in a rain storm, a glowing fireside in a blizzard, antitoxin in infection, are all attempts to produce *anoci-conditions*. In the beginning, however, man, in common with most animals, had but two principal methods of self defense against the dangers which surrounded him—he fought or he ran away. There is strong evidence that the animals most capable of being shocked are those whose self-preservation originally depended upon some form of motor activity. In man and other animals, this motor activity expresses itself in running and fighting; hence the motor mechanism comprises the muscles and the organs that contribute to their activity.

Motor activity, then, is excited by adequate stimulation of the nerve ceptors both of the *contact* ceptors in the skin and of the *distance* ceptors or special senses. They assume that excessive stimulation of the *distance* ceptors (special senses) is as potent as excessive stimulation of the *contact* ceptors in producing shock. As has already been indicated, they assume also that the environment of the past (phylogeny), through the experiences of adaptation to environment, predetermines the environmental reactions of the present. It is, therefore, the motor mechanism in particular through its phylogenic association with injury to the individual that is responsible for the discharges of energy which are occasioned by the *presence* or even the *thought* of danger. These stimuli, when intensive enough or protracted enough, produce the extreme conditions called "exhaustion" and "shock." In other words, this type of shock is caused by *excessive stimulation of the mechanism of energy transformation*. Stimuli of sufficient intensity inevitably cause exhaustion and may cause death. If the functional activity of the brain cell, resulting from responses to stimuli, takes the form of obvious work performed, such as running, the phenomena expressing the depletion of the vital force are termed *physical exhaustion*. If the stimuli are so intense that the brain cells become so damaged as to be unable to perform their work, the condition is commonly designated as shock.

ANOCIATION. Their practical application of the kinetic theory of shock in the development of the shockless operation through *anoci-association*, or *anociation* (as they now prefer to call it), also will bear repetition. Every adequate stimulus, whether from trauma or emotion, predisposes to shock. That is to say, the sight of the operating room, the spoken word implying danger, the taking of the anesthetic, the



instrumental injury of the tissues in the course of the operation, and the irritation of exposed divided nerves in the fresh wounds, are all injurious stimuli. Obviously, the only practical method of protecting the brain is the development of an operative technic which will exclude from the brain the stimuli of the special senses and of common sensation, and the employment of an anesthetic agent that does not harm, but rather acts as a protection to, the brain cells. They illustrate the principle of *anociation* by a survivor of the wrecked Titanic who, if he had been anesthetized in his bed before the accident, and, while still unconscious, carried on deck and lowered into a life boat and

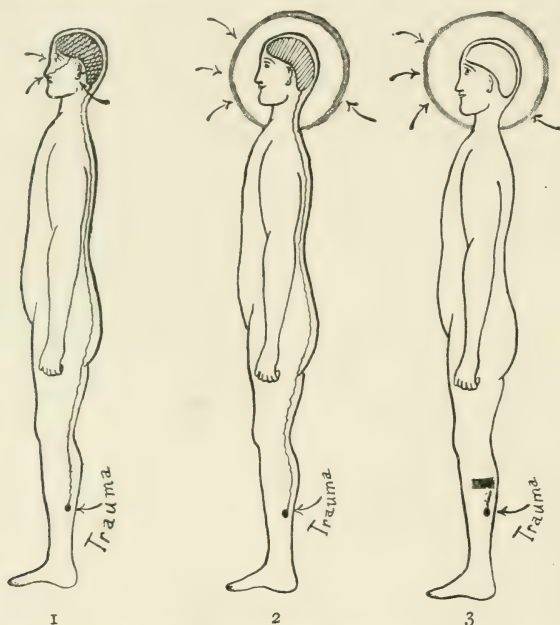


FIG. 33.—Schematic drawing illustrating protective effect of anociation. 1, Conscious patient in whom auditory, visual, olfactory and traumatic noci-impulses reach the brain; 2, patient under inhalation anesthesia in whom traumatic noci-impulses only reach the brain; 3, patient under complete *anociation*; auditory, visual and olfactory impulses are excluded from the brain by the inhalation anesthesia; traumatic impulses from the seat of injury are blocked by novocain.

taken aboard the rescue ship without being allowed to waken until he was safely in bed in a comfortable state-room, would have passed through the stormy sea in a state of *anociation*. There is no single anesthetic that will exclude all the harmful physical and psychic stimuli from the brain. Local anesthetics protect the brain from the effects of local or operative injury, but they do not protect the brain against destructive psychic strain. Inhalation anesthetics exclude the psychic stimulation of the brain cells but do not exclude the operative or traumatic stimulation. They, therefore, do not advocate ether alone, chloroform alone, or nitrous oxide alone; nor advocate local anesthesia alone, morphin alone, or spinal anesthesia alone, but through selection

and combination of anesthetics aim to secure the anesthesia that in a case in hand will exclude all stimuli from the brain and thereby obtain *anociation*.

The *anociation* should begin with the pre-operative environment. In other words, the work of the surgeon does not begin in the operating room, but the operating-room, the process of healing and the patient must be considered as a whole. The surgeon, the members of the house staff, the hospital superintendent, the intern, the nurse, the orderly—every one who comes in relation with the patient—must bear

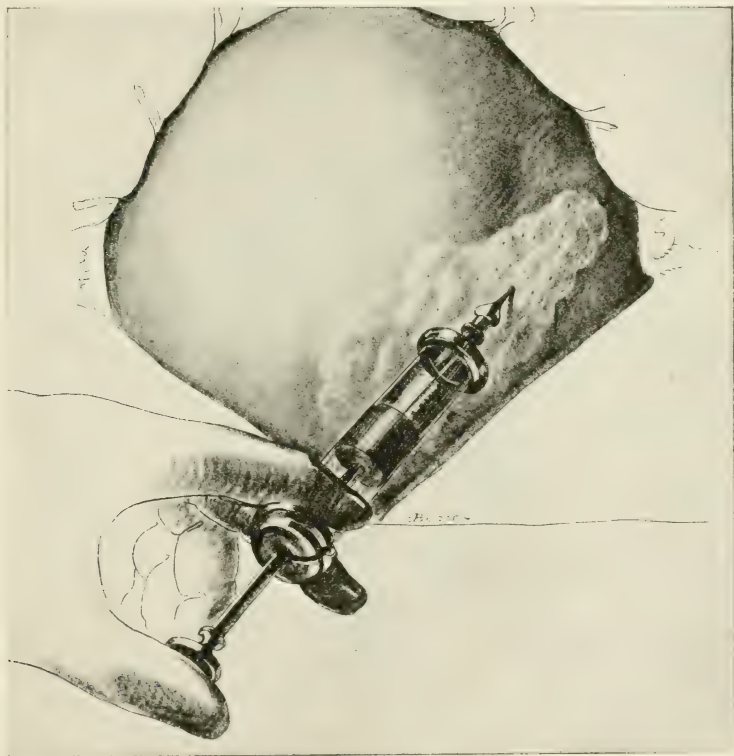


FIG. 34.—Infiltration of novocain between superficial and deep layers of skin. Note "pig-skin" appearance.

in mind that even comparatively slight factors may contribute—even mightily—to the ultimate welfare of the patient. Already we have come to realize to some extent that human beings are integral organisms and that one integral part cannot suffer without the suffering of most of all the rest. The reverse is also true, that any factor which contributes to the welfare or improvement of one part also contributes to all the rest. They emphasize the importance of the emotional factor in producing shock. If the natural fear of the approaching ordeal, felt by every normal individual, be augmented by tactless words in the surgeon's consulting-room, by an ungracious reception at

the hospital, by inconsiderate treatment by a nurse or orderly, by the sound of clanking instruments, or by the rough or forced administration of an anesthetic, avoidable insult is given to the nervous mechanism and this is added to the lowered resistance of the patient resulting from his diseased condition. By an assuring pre-operative environment; by a definite dulling of the nerves through the administration of a narcotic; by a non-suffocating odorless inhalation anesthetic; by a local anesthetic to cut off all afferent impulses during the course of the operation; by gentle manipulation and sharp dissection which not only means minimum pain but minimum trauma, cell destruction and extravasated blood [which eventually become toxic agents and thus

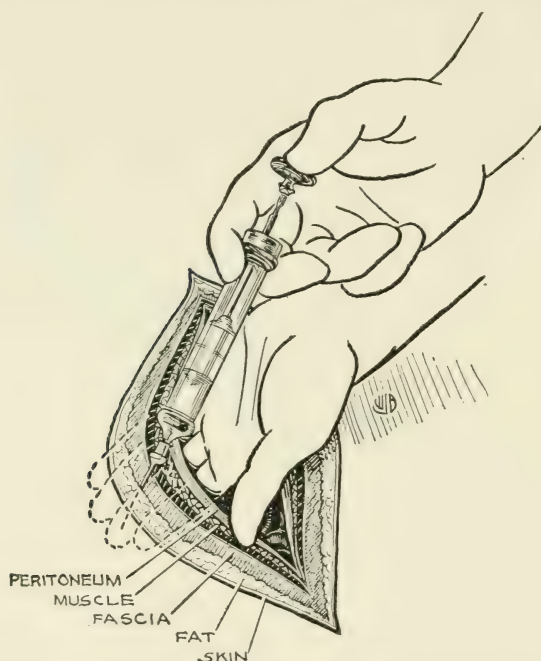


FIG. 35.—Abdominal operations: Infiltration with quinin and urea hydrochloride at a distance from the incision.

chemical factors in the production of circulatory failure—Reviewer], by the combination of all these methods the patient is protected from damage from every factor except those which exist in the diseased condition.

**GENERAL TECHNIC OF ANOCIATION.** *Morphin and Scopolamin.* To mitigate the preoperative anxiety, facilitate the induction of anesthesia and diminish the damage to the organs of the kinetic system by trauma, morphin, grain  $\frac{1}{6}$ , and scopolamin, grain  $\frac{1}{150}$ , are given an hour before the operation to all patients, except the aged and the very young and those whose feeble condition contra-indicates the use of a narcotic.

*General anesthesia* is induced by nitrous oxide, oxygen anesthesia.



*Novocain.* Every division of a sensitive tissue, that is, of a tissue supplied with noci ceptors, is preceded by the injection of novocain in 1 to 200 solution with adrenalin, except in exophthalmic goiter cases.

They emphasize certain points of prime importance to be observed in the induction of local anesthesia. No nerve filament should be omitted. The infiltrated parts should be subjected immediately to pressure, as firm pressure with the hand greatly increases the efficiency of the anesthetic. The first infiltration should be between the superficial and deep layers of the skin in such a manner as to cause a pig-skin appearance (Fig. 34). This is facilitated by putting the skin on tension and then, while making the injection, pushing the needle along in the skin parallel to the surface. Nerve blocking is of value in operations on the chest, the abdomen, the jaw, for hernia, and for goiter. The anesthetic solution should be most carefully prepared and sterilized. To normal saline solution prepared with distilled water and boiled for twenty minutes is added a sufficient number of novocain crystals to make a 1 to 200 solution, which is then boiled for ten minutes each on two successive days; when novocain is properly injected it anesthetizes the part immediately; the anesthesia lasts approximately an hour and it does not interfere with wound healing. The incision through the skin is made strictly within the infiltrated area, the razor-edge knife dividing the skin and underlying fat. As fat is but sparsely supplied with nerves, this tissue may be divided down to the fascia without further infiltration. The fascia is next infiltrated then divided, and in succession the other tissues are anesthetized, layer by layer, before they are divided.

**SECONDARY WOUND SHOCK.** Secondary wound shock, according to the definition of Bayliss, is a condition of circulatory failure caused by factors other than nervous, *i. e.*, traumatism, infection, toxemia anesthesia and hemorrhage, and, instead of coming on immediately, it develops after an interval of several hours.

*Hemorrhage.* As a cause of circulatory failure, hemorrhage needs no explanation. But the fact that this definition of Bayliss's eliminates the supposed need of differentiating between shock and hemorrhage at least simplifies the problem. Instead of considering them two distinct phenomena, their relation to each other is one of cause and effect.

*Toxemia.* Last year we reviewed the experience of Cannon, Delbet and Quenu<sup>15</sup> with war wounds, and their experimental and clinical demonstration of the production of circulatory failure by chemical substances obtained from traumatized and devitalized tissues. Cannon,<sup>16</sup> in a series of experiments, found that the shock-like state, which in the controls invariably followed the crushing of a limb, could be entirely avoided by blocking the circulation draining that part. This experimental work was accepted by the English Research Committee and would seem to be conclusive proof of the importance of traumatic toxemia as a cause of circulatory failure in traumatic wounds.

<sup>15</sup> Lee: PROGRESSIVE MEDICINE, December, 1919, p. 210.

<sup>16</sup> Lancet, 1919, cxcvii, 137.

Crile, in a personal communication, said he had repeated these experiments, both in man and in animals, and had not been able to prevent circulatory failure by the application of a tourniquet proximal to the traumatized area, but that he had always succeeded when he blocked the spinal cord with spinal anesthesia. This, however, is not in accord with the experience of most of the workers. McCartney<sup>17</sup> believes that his traumatic toxemia is one of the important etiological factors in secondary wound shock.

Turek<sup>18</sup> expresses the opinion that traumatic shock is caused by the toxins liberated from the wound itself. His investigations apparently explain why débridement, which removes the devitalized tissues from the wound, prevents the poison of the dead tissues from spreading cell destruction to the normal tissues. Primary suture restores the circulation of the injured part and puts a stop to further cell necrosis. The traumatic shock syndrome follows whenever destruction of tissues takes place. In the laboratory, shock may be produced by simple ligation and cutting off the blood supply to the part. The interruption of the circulation prevents the nourishment of the tissues below the ligature. Cell necrosis promptly follows. The changes taking place in the cell and tissue under these conditions have been described by Virchow. Experimentally, tissue was taken from a limb of an animal so treated. A suspension in salt solution made of tissue taken immediately after the application of the ligature to the main vessel, when injected subcutaneously into the animal had no injurious effects. After an interval of three hours, a frozen section of tissue from the same area showed evident necrotic changes and an emulsion in saline, prepared in the same manner as before, produced the syndrome of shock with a fall of blood-pressure and temperature, and, finally, death. The autopsy which was performed immediately showed the most marked feature to be splanchnic stasis. Sections of the liver, lung and upper alimentary tract showed that the blood had stopped in the pulmonary zone of the lung, the portal zone of the liver and the submucosa of the upper alimentary tract. In another animal the leg was gently massaged after the removal of the ligature, so that the disintegrated or modified albumins of the necrosed tissues of the leg might be thrown into the general circulation. This was at once followed by the syndrome of shock, and death occurred within a short time.

Naedelai<sup>19</sup> experimentally demonstrated that aseptic, crushed, devitalized tissues are definitely toxic when implanted into normal tissues, thus corroborating the work of Delbe and many others, and confirming the clinical observation for the necessity of débridement.

Quenu<sup>20</sup> reports investigations on the toxicity of lacerated muscles. In the experimental production of shock, he removed the crushed and

<sup>17</sup> Edinburgh Medical Journal, 1919, xxiii, 157.

<sup>18</sup> American Journal of Surgery, 1920, xxxiv, Anes. Supp. 6.

<sup>19</sup> Zentralbl. f. Chir., Leipzig, December 6, 1919, No. 49, vol. xlv.

<sup>20</sup> Academy of Sciences Parish, Journal of the American Medical Association, 1919, lxxii, 925.

lacerated muscles of rabbits, rats, mice, eels and frogs, injecting the filtrate of these tissues into other animals. Toxic effects were noted in every instance which was similar to the phenomena of shock and frequently terminated in death. The toxic effects were always of the same type, varying greatly in intensity.

Dale-Laidlaw-Richards<sup>21</sup> work with *histamin*, was also reviewed last year. They produced a characteristic shock-like condition when this substance was introduced by injection into the circulation of animals and they found that the pathological changes in this experimental secondary toxic circulatory failure or shock consisted in a dilatation of the capillaries and an escape of blood plasma into the tissues. The result of these changes was a diminished volume of the circulating blood (fall of blood-pressure) and a concentration of the corpuscles in the capillaries. This concentration of the blood has been previously referred to by Crile and Sweet and was called by Cannon, Exemi. Abel<sup>22</sup> was able to recover histamin, or a very similar substance, from almost every type of mutilated human tissues and this would seem to complete the experimental demonstrations that circulatory failure can be caused by the absorption of chemical substances, of the nature of histamin, from traumatized and devitalized human tissues. This type of circulatory failure consists in a decrease of the circulating blood volume the result of an escape of the blood plasma into the perivascular tissues and of a stasis in the capillaries.

Krough<sup>23</sup> has collected sufficient evidence to justify his statement that the capillaries contain contractile elements of some sort within themselves which explains the enormous variations in permeability of the capillary zone. Dale and Richards's work with histamin assumes that such changes occur in the capillary circulation in shock, and this demonstration of independent activity on the part of the capillaries would seem to be the connecting link in the explanation of shock that is based upon circulatory failure.

A decrease in the circulating blood volume whether due to actual loss of blood, as in hemorrhage, or a relative loss of blood within the vessels, as in capillary stasis and transudation of the plasma into the perivascular tissues, results in a decrease in the number of circulating red blood cells and thus a diminished oxygen supply to the body tissues and a consequent impairment, or destruction, of their functions. The impairment or loss of function of the body tissues is in truth "an unhinging of the machinery of life" and is the condition which we know as shock. This is practically the working hypothesis we suggested in last year's review<sup>24</sup> and all the literature since then would seem to confirm it.

Although it is easily conceivable that histamin might arise from the breaking down of the amino-acid histidin, which is an integral complex of the tissue proteins, there is still no proof that histamin is in fact

<sup>21</sup> Lee: *PROGRESSIVE MEDICINE*, December, 1919, p. 209.

<sup>22</sup> Journal of Pharmacology and Experimental Therapy, Baltimore, 1919, No. 3, xiii, 243.

<sup>23</sup> Journal of Physiology, May 20, 1919, lii, 457.

<sup>24</sup> *PROGRESSIVE MEDICINE*, December, 1919, p. 210.



the substance responsible for the capillary damage and altered permeability in traumatic toxemia. But for the present it represents a convenient agent for the experimental production of shock through chemical influence on the bloodvessels and Dale<sup>25</sup> has been further enabled, by its means, to study the influences of other factors in the genesis of shock following traumatic toxemia. Exhaustion, pain, cold, thirst, hemorrhage and anesthetics have all been supposed to play some part in the production of circulatory failure. Dale has found that some of these factors, which lend themselves to experimental investigation, lower the normal resistance to the poisonous histamin. This is particularly true of a large, but not essentially serious, hemorrhage. It is likewise true of anesthetics, ether and chloroform being markedly more harmful than nitrous oxide and oxygen. Dale feels that it is probable that the normal resistance of healthy subjects to the toxic products of traumatized tissues is probably quite high, and that, in animals at least, it is demonstrable that chloroform or ether are more dangerous because of their greater depressing effect upon the normal resistance than nitrous oxide and oxygen. Dale further suggests that the greater safety in civil surgery of the combination of local anesthesia with nitrous oxide and oxygen, as compared with prolonged anesthesia with ether or chloroform, may find its true explanation along the same lines. Thus, Dale feels that in cases in which bacterial or other toxic agents are present, chloroform and ether should be avoided whenever possible.

**Blood Transfusion.** The transfusion of blood is at the present time considered the most valuable method of restoring blood-volume. This almost universal experience during the war is being confirmed in civil practice as the method is being more generally applied.

Furness and Lee<sup>26</sup> state that the transfer of the vital fluid of a vigorous, healthy human to one stricken with disease has been conjured with from the time of the earliest medical records. In 1492, three youths are said to have lost their lives as a result of an unsuccessful attempt to save the life of Pope Innocent VIII by blood transfusion. With Harvey's discovery of the mechanism of the circulation of the blood, renewed interest developed in the procedure, and Richard Lower, in 1666, was reported to have made the first successful transfusion by means of a goose quill. The syringe method of Ziemssen and all of the indirect methods now in use were devised by some surgeon and then forgotten before Carrel and Crile perfected the first practical method of direct transfusion by anastomosis of the bloodvessels. The gradual simplifying of the technic by Payr, Elsberg, Ottenberg, Levin, Lespinasse, Soresi, Bernheim, Kimpton, Vincent, and many others, and the removal of the danger of agglutination and hemolysis, resulting from the research of Moss upon the blood groupings, had, before the onset of the war, given a distinct impetus to the procedure.

Unger feels that the indications for transfusion extend further than that of the restoration of blood-volume.<sup>27</sup> His indications are: (1)

<sup>25</sup> British Journal of Experimental Pathology, April, 1920, i, 103.

<sup>26</sup> Pennsylvania Medical Journal, July, 1920, p. 577.

<sup>27</sup> Journal of the American Medical Association, 1919, lxxiii, 815.

Hemorrhage; (2) shock; (3) disease of the blood; (4) toxemias; (5) infections; (6) general debility.

*Hemorrhage.* Transfusion of blood serves not only to replace the actual loss of blood but also to act as a hemostatic, checking the actual cause of bleeding.

*Shock.* He is not quite as positive about its value in shock; this is probably because of his lack of experience with war wounds.

*Reinfusion of Blood in Acute Hemorrhage.* Von Arnim<sup>28</sup> reports 12 cases of tubal abortion in which the reinfusion into a vein of from 300 to 1000 c.c. of the woman's own blood diluted with an equal amount of physiologic sodium chloride solution and a little sodium citrate. The blood was scooped or soaked up from the abdominal cavity and passed through a funnel over some gauze as a filter, from the filter the blood passed into a receptacle containing the salt solution and sodium citrate. She reports that the patients recuperated from their moribund condition with unusual rapidity. Intense cyanosis and attacks of pain in the chest, with dyspnea and a chill, occurred in 2 cases. She suggests that the toxic effects in the dying blood might explain these by-effects. We have had personal experience during the last year with this procedure but have limited the blood used to that which can be aspirated from the abdominal cavity into a flask by means of a rubber tube. In this way large clots were avoided, but most important, untraumatized blood only was obtained.

Kulen Kampff<sup>29</sup> reports the reinfusion of extravastated blood in 9 cases of intra-abdominal hemorrhage and refers to its 35 other cases on record.

Friedemann says he has been using this technic for several years and has never noted any signs of intoxication with it.

*Disease of the Blood.* In secondary anemia, blood transfusion is satisfactory, provided the primary cause is removed. In pernicious anemia it probably never permanently cures, but it yields results superior to those obtained by any other method of therapy. By repeated transfusions, remissions can be effected and the lives of some patients made useful for years. Hemophilia is not cured by transfusion, but the bleeding is practically always controlled. It will succeed when all other methods fail. In purpura hemorrhagica the results are very good; repeated transfusions are often necessary to control the bleeding. In acute lymphatic leukemia only a temporarily favorable result can be secured by transfusion. In bleeding of the newborn, transfusion is a specific.

Last year we called attention to the use of the longitudinal sinus for transfusion in infants. Several reports are found in this year's literature of the successful application of this method.

*Toxemias.* Transfusion has been used for some time in a limited number of toxemias. It should be more generally used in the toxemia of pregnancy and in the toxemias associated with pneumonia and typhoid fever.

<sup>28</sup> Zentralbl. f. Gynäk., Leipzig, November, 1919, No. 48, vol. xliii.

<sup>29</sup> Ibid.



*Infections.* In localized pyogenic infections, transfusion will increase the patient's resistance and aid in overcoming the infection. In bacteremia, when the source of the organisms can be found and eliminated, the results are excellent, as in cases of sinus thrombosis following mastoiditis in which the jugular vein has been ligated.

*General Debility.* Transfusion, when used as a supporting measure preliminary to operation, lessens the first operative mortality.

Polak<sup>30</sup> has found, notwithstanding the poor results reported by Linderman and Garbat, in their blood transfusions of postoperative septicemia in general surgical cases, found that the use of small repeated transfusions of blood has been of distinct value in the treatment of bacteremia and thrombophlebitis following puerperal infection. Transfusion in infection seems to serve the double purpose of lessening the secondary anemia and supplying normally active leukocytes for temporary defence. Small transfusions of blood, 250 to 300 c.c., are given every third day. The preliminary administration of one-third grain of morphin has been found to materially diminish the severity of reaction when citrated blood is used. Some reaction occurs in 60 per cent. of cases. Detailed blood studies made before and after each transfusion demonstrated that the leukocyte count was invariably increased and the blood-pressure raised by the treatment, temporarily the number of red cells and the hemoglobin were also increased, but rapidly decreased in the succeeding forty-eight hours.

**TRANSFUSION OF ANTIBACTERIAL BLOOD.** Little,<sup>31</sup> in a case of *Staphylococcus pyemia*, transfused blood from a donor who had been injected with vaccine made from the *staphylococcus* culture obtained from the patient. Three or four days before each transfusion the donor was "primed" with a vaccine obtained from the patient. This antibacterial blood from the donor was transfused four times during four weeks. The fact that the patient recovered from innumerable abscesses of the soft tissues of the ankle-joint, left hip-joints, left knee-joint, a resection of the rib for a lung abscess, gives one an estimate of the gravity of the infection. Those in professional attendance reached the conclusion that life was saved by the transfusions. Possibly blood without attempted action with the patient's vaccine might have accomplished the result. However, it is rational to conclude that the patient's vaccine injected into the donor produced antibodies in the blood which were of specific value to the patient in overcoming her septicopyemia.

**PLASMA THERAPY.** Terrein<sup>32</sup> found that in a case of malignant measles in which the child's death seemed imminent on the fifth day the transfusing of 20 c.c. of whole blood from a brother who had had measles six months before caused a miraculous change for the better. Terrein introduced this blood subcutaneously. He points out that the subcutaneous route avoids the danger of shock from intravenous administration, and it also renders unnecessary any preliminary testing of the donor's blood for hemolytic properties.

<sup>30</sup> Am. Jour. Obst., 1919, lxxx, 291.

<sup>31</sup> Journal of the American Medical Association, March 13, 1920, No. 11, lxxiv, 73.

<sup>32</sup> Bull. de la Soc. méd. des hôp., Paris, December 26, 1919, No. 38, xliii, 1134.



Though there is a general agreement among surgeons as to the present safety of the procedure, and the increasing indications for its use in conditions other than the restoration of the loss of blood-volume, actual or relative, there is still a decided difference of opinion as to the relative value of whole blood or blood altered by the addition of some anti-coagulant like sodium citrate.<sup>33</sup> The essential difficulty in the performance of blood transfusion is, of course, the element of coagulation. In all of the methods which have been devised, both direct and indirect, effort has been directed toward minimizing the trauma to the cellular blood elements. Protecting the blood from the drying effects of the air, the making of the contact walls of the intermediate system as smooth as possible and the minimizing of the injury to the walls of the bloodvessels, were all found necessary to prevent the formation of the coagulating substance, thromboplastin, which is liberated when tissue cells are injured.

Coagulation of the blood, according to Howell, depends on the disturbance of the normal balance in the blood plasma of substances which he calls antithrombin and prothrombin. Normally, antithrombin binds the prothrombin and renders it inactive and unable to start coagulation. But whenever there is cell injury of any kind to the tissues, the blood cells or the platelets, a substance called thromboplastin is set free which neutralizes the antithrombin and thus liberates the prothrombin which then combines with calcium salts to form thrombin. The free thrombin coagulates the fibrinogen, giving rise to a normal blood clot. All efforts prior to the work of Hooker, in 1913, were directed toward the prevention of the formation of thromboplastin. Hooker suggested that a physiologic agent of the nature of antithrombin be used to coat the contact surfaces of the intermediate system employed for the transfusion, and successfully used a solution of hirudin, which was obtained from the leech. In 1914, Agote, Hustin and Lewisohn suggested the addition of a chemical to the donor's blood which would prevent coagulation by neutralizing the thromboplastin which might be formed when the blood was passed through an indirect system. By the addition of sodium citrate to the donor's blood, after it had been withdrawn, they found that coagulation could be delayed for long periods of time. A concentration of 0.2 per cent. was found to preserve the blood for hours, and, in France, Tuffier reports that citrated blood has been kept in the refrigerator for as long as twenty-six days and was apparently just as useful after that lapse of time as fresh blood. Prior to this work, anti-coagulants of a chemical nature were considered impractical because of their well-known toxic qualities, but it is claimed that this weak solution of sodium citrate is so slightly toxic to human tissues that it can be used with impunity.

The elimination of the element of coagulation, in the transfusion of blood, by the addition of a chemical, has made possible such a simple technic that it has revolutionized the whole procedure and at first apparently promised to supersede the use of whole blood. In spite of

<sup>33</sup> Furness and Lee: *Loc. cit.*

the claims of those enthusiastic about the citrate method, the consensus of opinion of the Inter-Allied Surgical Congress, in 1918, based on the personal experience of such men as Crile, Tuffier, Depage and Makins was that, in their opinion, whole blood gave more satisfactory results than the citrated.

Crile and Lower,<sup>34</sup> while admitting the greater simplicity of the citrate method, are so firmly convinced that whole blood is preferable that they urge that every effort should be made to overcome the increased difficulty of the technic and to provide the necessary supply of donors to make this method at all times available.

Losee states<sup>35</sup> that though the citrate method has gained its popularity on account of the facility with which it is performed, there is no reason to believe that it is as beneficial to a patient as the unmodified blood which is not subjected to a chemical change and which is out of the body but for a short time. It is indeed quite true that citrated blood is entirely efficient in patients suffering from acute hemorrhage when volume only is needed, but, with patients who have had a severe anemia for some time and are in poor physical condition, the method which will accomplish the best result with the least possible tax on the already poorly functioning organs of the patient is the one to select.

Huck<sup>36</sup> has shown that there is no constant physical change after the transfusion of blood and no mechanical effect can be shown to follow the introduction of definite quantities of blood, but he considers the effect essentially a biologic one. This too seems to be an argument in favor of the use of blood free from any foreign chemical.

That none of the various methods so far devised for the indirect transfusion of whole blood are entirely satisfactory is amply proved by the many suggestions that have appeared in the literature of this past year. Losee<sup>37</sup> feels that the Lindeman syringe cannula method, where the operator, assistant and nurse work perfectly together, is the nearest approach to a direct transfusion that can be obtained, and therefore the advantage of both the direct and the indirect methods are combined.

Abelmann<sup>38</sup> employs an ointment containing 10 per cent. of sodium citrate with the syringe method, with the object of providing an effective anticoagulant as well as a lubricant for the piston. Stanley<sup>39</sup> has devised an apparatus of the ball-valve type which can be used with a Luer syringe of any capacity (Fig. 36). When the plunger of the syringe is drawn out, ball *A* engages in the socket, preventing the passage of fluid, while ball *C* is displaced upward to position *B*, allowing the blood to come from the donor into the syringe. When the syringe piston is pushed in, the ball in the lower chamber engages in the socket at *C*, preventing the fluid from returning to the donor, at the same time ball *A* is released from its socket and assumes a position in the upper chamber at *D*, allowing the blood forced from the syringe to flow into the veins of

<sup>34</sup> Surgical Shock, Saunders & Co., 1920.

<sup>35</sup> American Journal of the Medical Sciences, November, 1919, vol. clviii.

<sup>36</sup> Johns Hopkins Bulletin, 1919, xx, 63.

<sup>37</sup> Loc. cit.

<sup>38</sup> Medical Record, September 1, 1918.

<sup>39</sup> Journal of the American Medical Association, 1920, lxxiv, 671.

the recipient. The balls engage by gravity and the valve must be held in a vertical position. The arm of the recipient, therefore, must be slightly higher than that of the donor. The syringe and attachments are sterilized and the interior of the syringe is coated with Abelmann's citrated ointment.

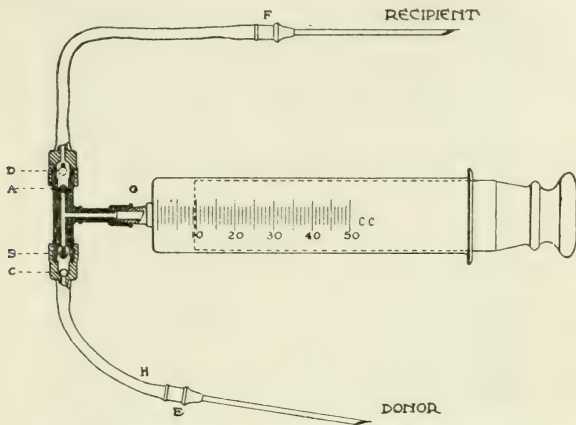


FIG. 36.—Details of blood transfusion apparatus. (Stanley.)

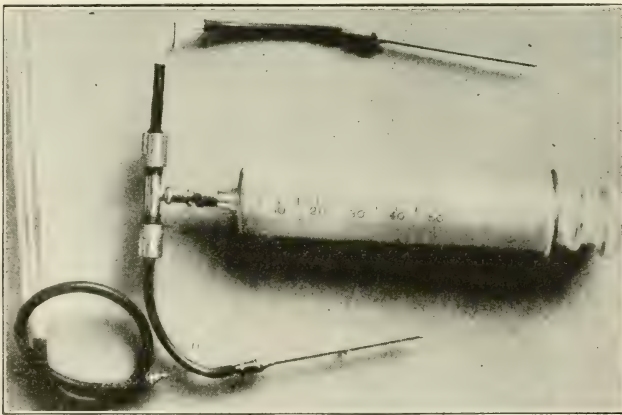


FIG. 37.—Blood transfusion apparatus and buret. (Stanley.)

James<sup>40</sup> reports that after repeated experimentation with the ball valve, in which balls of various metals and specific gravities were used, the principle was found to be unreliable because it was not leak-proof. The balls do not fall in position in their respective sockets to shut the valve completely, thus frequently causing leakage and back flow, so that one is not certain whether the blood has come from the donor or recipient, or *vice versa*. Stanley himself speaks of the necessity of having several sets of the valves at hand, so that another can be

<sup>40</sup> Journal of the American Medical Association, July 24, 1920.



substituted as soon as the valves stick with coagulated blood. We feel sure that this ball-valve principle is impractical unless citrated blood is used, for whole blood will not submit to such trauma without rapid coagulation resulting. James's modification of this apparatus

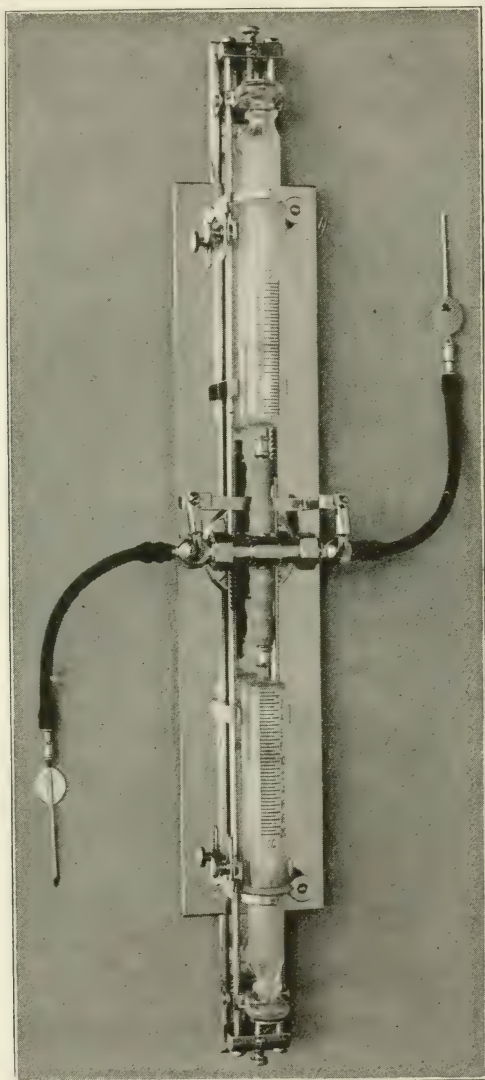


FIG. 38.—Combined blood transfusion and aspirating machine. (James.)

provides a means for supporting and operating opposed Luer syringes. The machine is so constructed that each pump cylinder, which is a 10 to 20 c.c. Luer syringe, may be quickly and easily disconnected independently of the other cylinder and piston. In the center of the base plate and extending transversely and midway between the syringe nozzles

is a tubular member which contains the conduits and valve chambers. The tubular member is provided with two oppositely extending nipples midway between its ends and in alignment with the nipples on the nozzles of the syringe barrels. The nipples of the syringes and those of the conduit chamber are connected by a short length of rubber tubing. By this apparatus a continuous flow of blood from donor to recipient may be obtained and accidental back-flow is impossible. He says that the apparatus has been used successfully at the Gouverneur Hospital for both blood transfusion and aspirating purposes. It would seem that the same criticism, though probably to a lesser degree, would apply



FIG. 39.—Transfusion tube devised with the aid of the staff of a casualty-clearing station. (Capacity, 450 c.c., made by Gentile, Paris.)

to this apparatus. It might work with citrated blood but the trauma received by the blood-cellular elements passing through such a complicated apparatus would in a short time result in coagulation unless some anticoagulant were introduced.

The same criticism applies to Unger's apparatus, which is composed of two Luer syringes and a metallic three-way valve arrangement. The other type of apparatus consists of various shaped paraffin glass receptacles, one end of which is drawn to a point small enough to introduce into the veins of the donor and recipient. Vincent, French and Kimpton-Brown have all devised very good models. At the present time paraffin-





bring about cessation of hemorrhage, citrated blood may serve as a substitute.

Lewisohn<sup>43</sup> reports his latest technic and outfit for the transfusion of blood with the aid of sodium citrate. The outfit consists in (Fig. 41):

1. Two glass ampoules each containing 50 c.c. of a 2.5 per cent. sterile solution of sodium citrate (*l*).
2. Two glass graduated jars (500 c.c. each) (*h*).
3. Two small glass graduated jars (50 c.c. each) (*i*).
4. One glass rod (*k*).
5. One salvarsan flask (*g*).
6. Two cannulae (one large size and one medium size) (*a b*).

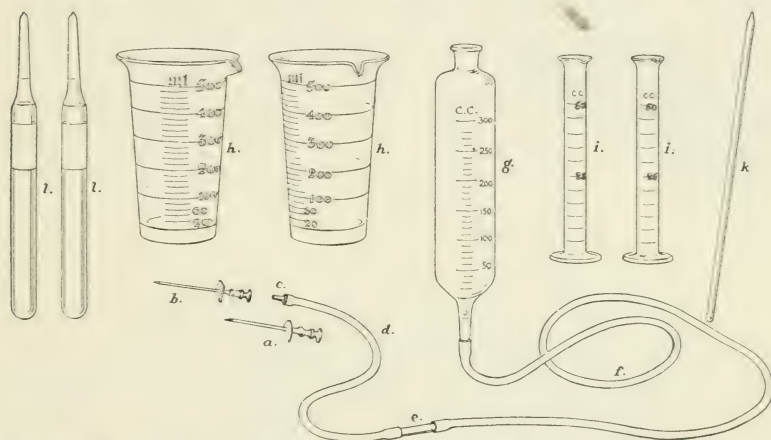


FIG. 41.—Complete outfit for transfusion of blood with the aid of sodium citrate; *a* and *b*, cannulae; *g*, salvarsan flask with rubber (*d f*) glass taper connect (*e*) and adapter (*c*); *i*, small glass jars; *h*, two large glass jars; *k*, glass rod; *l*, two glass ampoules containing 50 c.c. of a sterilized 2.5 per cent. solution of sodium citrate. (Lewisohn.)

The technic consists of two separate steps: (1) The taking of the blood from the donor, and (2) the injection of citrated blood into the recipient. The first step represents a simple venesection and a mixture of the blood with a citrate solution; the second step is an intravenous infusion. Farr<sup>44</sup> uses a 1-liter Erlenmeyer flask adapted for this purpose Fig. 44.

In *recapitulation*, blood transfusion is the optimum procedure in circulatory failure where the loss of blood-volume is actual, as in hemorrhage, or relative, as in shock. The fact that this procedure is in no sense a mechanical reaction but in every sense a biologic one, more than justifies its use as a therapeutic measure in diseases of the blood. Whole blood, when obtainable, is generally considered to be the most effective. The indirect method is the only one to be considered, and, at the present time the use of paraffined glass receptacles of the type of the Kimpton-Brown tube is the most practical. Of the many modifications of this tube and the various methods devised as substitutes, all fail to

<sup>43</sup> New York State Journal of Medicine, December, 1919, No. 12, xix, 431.

<sup>44</sup> Surgery, Gynecology and Obstetrics, March, 1919, p. 327.

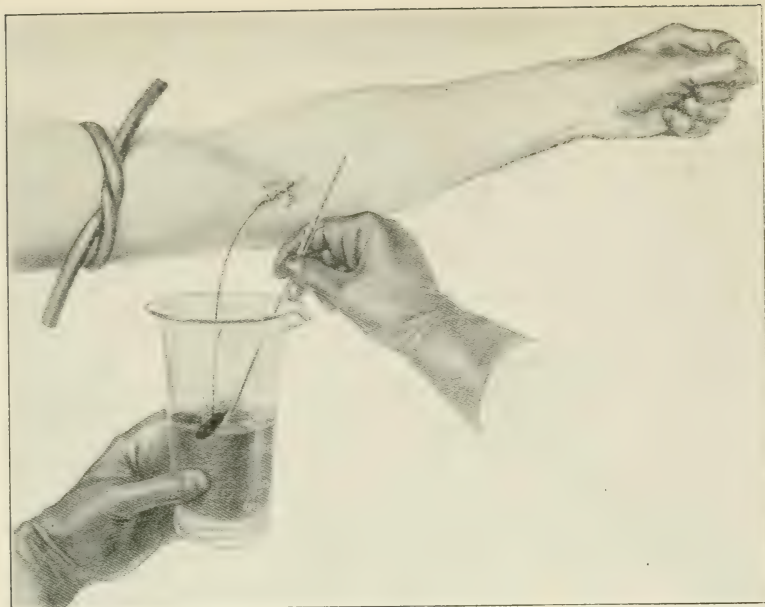


FIG. 42.—Taking blood from the donor. (Lewisohn.)

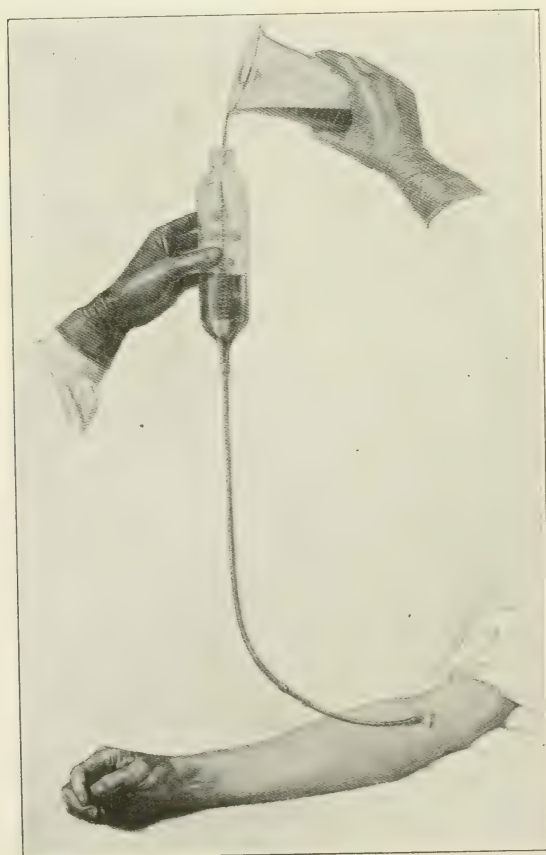


FIG. 43.—Infusion of citrated blood into the recipient. (Lewisohn.)

answer to the test of simplicity. The citrate method, as described by Lewisohn, has not been improved and can be substituted for whole blood in case of hemorrhage or when it is not practical or possible to use unmodified blood.

Last year we reported the suggestion of Sanford<sup>45</sup> that dried cover-slip preparations of blood could be used in determining the blood group of individuals under consideration for transfusion. Such preparations could be sent to laboratories at a distance, or dried preparations on filtered paper could be sent by the laboratory and used at the bedside in choosing the proper donors.

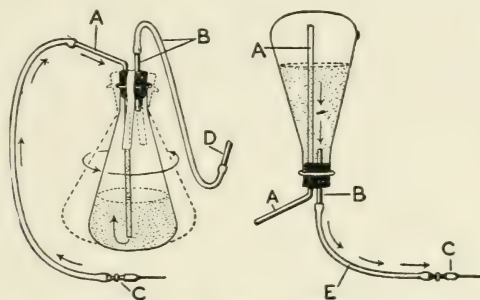


FIG. 44.—(Farr, Gilroy.)

Karsner and Koeckert<sup>46</sup> describe the deterioration of normal human iso-agglutinins within from two to three weeks, and a loss of group specificity within from three to five weeks after the drying of the serum.

Owing to the practical importance of this subject in view of the wide adoption of Sanford's method of using serum on dried cover-glasses, Kolmer<sup>47</sup> reports some studies which he undertook. He had felt for some time that Noguchi's method of drying rabbit antihuman serum in filter paper yielded less agglutination of the corpuscles in the conduct of complement-fixation tests than serum preserved in the fluid state. He then made studies of the influence of hemagglutinins and hemolysins in normal human serums for the corpuscles of persons and certain of the lower animals, of drying the serums at room temperatures on cover-glasses, as described by Sanford, and in filter paper as described by Hartman. The general results of these investigations were to show that both hemagglutinins and hemolysins in normal human serums frequently undergo considerable deterioration within the first to the fourth day after drying. However, when human serums containing large amounts of these hemagglutinins were chosen for drying on cover-glasses and properly preserved in a refrigerator, as described by Sanford, satisfactory agglutination tests were observed over a period of two or, three weeks at least. He feels quite sure that it is unwise to rely on the results of negative hemagglutination reactions with dried serums in the typing of blood, unless preliminary tests have shown that specific agglu-

<sup>45</sup> PROGRESSIVE MEDICINE, December, 1919, p. 214.

<sup>46</sup> Journal of the American Medical Association, October 18, 1919.

<sup>47</sup> Ibid., November 8, 1919.



tinins remain in the serum for at least a week after drying. He also calls attention to the practice of relying on agglutination tests alone for the matching of bloods prior to transfusion, and feels that the procedure is open to criticism.

In the course of investigation he found that hemolysins may be present in serums free of agglutinins for the same corpuscles, and it is possible that these isohemolysins may be responsible for some of the reactions following the transfusion of bloods free of agglutinins. For this reason he believes that tests preliminary to blood transfusion should include an examination for hemolysins as well as agglutinins, and that dried serums are not suitable in tests for the latter. He agrees with Karsner and Koeckert that undried serums put up in small capillary tubes are better adapted for the grouping of blood than dried serums; but since both hemagglutinins and hemolysins in normal serums are quite susceptible to heat, the serums should be kept at or near the freezing-point.

**The Surgical Hazard in Diabetic Patients.** Nellis B. Foster<sup>48</sup> points out that an increased surgical risk is generally recognized when the surgical disease is complicated by diabetes, but it is not so commonly appreciated that complications which might be regarded as surgical are the immediate cause of death in a large proportion of cases of diabetes. Thus a careful review of the records of two hospitals showed that of the fatal cases of diabetes dying beyond the third decade of life, about 60 per cent. of the fatalities occurred following operations. Of the surgical cases with a fatal termination, 70 per cent. die in coma. In attempting to estimate the severity of the disorder in this group of cases, the glycosuria was evidently the index. Accepting this standard for what it is worth, it was found that coma occurred after operation as often in mild cases of diabetes as in the apparently severe, which, of course, means that the estimations were made upon faulty criteria. Again, surgeons are accustomed to classify their operations as minor or major, and using these terms as commonly accepted we find that the mortality in diabetes patients is higher following minor operations than it is for major operations. Of course, major operations might not, as a rule, be attempted on diabetic patients, but this brings more into contrast the false estimate often placed upon the hazard of minor surgical procedures in diabetic patients.

Recent work with diabetes has shown the factors which go to make up the increased risk in surgical procedure and these factors can be analyzed and to a very high degree estimated. Glycosuria is not a reliable guide in the estimation of the severity of diabetes; in fact, it is doubtful if it is any guide at all further than a rough diagnosis. Glycosuria does not invariably connote true diabetes mellitus; on the other hand, the absence of glycosuria does not completely exclude the disease. The estimation of the severity of the disease depends upon the degree of hyperglycemia under varying conditions of diet. To appreciate the problem, the factors which influence the normal blood-sugar must be understood. Chief

<sup>48</sup> *Annals of Surgery*, March, 1920, No. 3, lxxi, 382.

among them are infections. Persons who are not afflicted with any metabolic disease show, when they are subjects of chronic infections, disturbances in the metabolism of sugar, and this disturbance is characterized by an increase of the blood-sugar beyond the normal limit after the ingestion of glucose and a prolongation of the blood-sugar curve beyond the normal two hours. Chronic infection in diabetic subjects induces a similar change which is clinically expressed in the difficulty experienced in reducing the hyperglycemia to normal by diet; moreover, this disturbance, produced by infection, implies on the part of the diabetic organism an increased difficulty in the metabolism of glucose, and, on that account, the tendency to acidosis is more marked. These fundamental facts are well exemplified in even minor infections in diabetic individuals. Thus, an acute attack of tonsillitis in the diabetic patient who, has probably acquired an ability to utilize carbohydrate without any abnormal change in the blood-sugar content, will, with the onset of such an infection, have sugar appear in the urine, even though he takes scarcely any food.

A decrease in the metabolism of glucose is manifested by some degree of acidosis, even after the infection has passed. It may require a considerable period of time before conditions are restored to what they were prior to the intercurrent infection. In children, relatively mild infections of this sort not infrequently lead to fatal acidosis and coma. These same changes in metabolism accompany the numerous infections which require surgical treatment—carbuncles, cellulitis. The next factor is the influence of anesthesia upon the carbohydrate metabolism. Every surgeon knows that glycosuria is occasionally manifested after anesthesia. Accompanying this disturbance there is more or less acidosis depending upon the nature of the operation and the period of the time of anesthesia. Thus, as with infections, we have a factor which aggravates and intensifies the peculiar disorder which characterizes diabetes. The third important factor is the predisposition of the diabetic to infections and a diminished recuperative power manifested by his tissues when infections are established.

A recognition of these facts should make it possible to determine when operation cannot be borne by a diabetic subject, also that it is possible to estimate the hazards entailed in border-line cases. The chief danger is always acidosis and coma, and, for that reason, a determination of this factor is the prime requisite. Estimations of the  $\text{CO}_2$  combining power of the blood give a very definite idea of the degree of acidosis. Normal blood shows a combined power above 55 per cent., severe degrees of acidosis are shown by a combining power of 20 per cent. or less. No diabetic patient has come to my knowledge who has successfully withstood an operative procedure whose blood shows a combining power of 30 per cent., and it is my opinion that less than 35 per cent. makes it too hazardous to attempt an operation. Forty per cent. is the lowest figure that permits a reasonable margin of safety for surgical procedures, considering the superimposed acidosis consequent upon the course of infection and the anesthetic. But the acidosis estimation is not all that is necessary, for many diabetics showing no acidosis, but with a blood-sugar



of over 35 per cent. succumb to operations because of acidosis that develops postoperatively, thus it is necessary to estimate the blood-sugar content as well as the degree of acidosis. Patients showing hyperglycemia of over 35 per cent., or a  $\text{CO}_2$  combining power of less than 40 per cent., cannot be expected to survive any operative procedure. The only safety with cases of this type is to change the metabolic state prior to the surgical treatment. If there is not time to do this, the case is hopeless.

The treatment of patients with diabetes preparatory to a surgical operation requires no departure from recognized principles. The object of the treatment is the restoration of, or an approach to, normal metabolism, and the index of success is the blood-sugar content and a  $\text{CO}_2$  combining power of the plasma. There is but one primary means to this end, dietetic, and it must be realized that in this disease food is a two-edged sword, and its use requires a nice scientific precision. The predisposing effect of infections to acidosis must never be overlooked. Fasting, which is hazardous unless controlled by constant laboratory test, is the most rapid and efficient method of decreasing hyperglycemia and acidosis. Unfortunately, when infections of a surgical character complicate the primary diabetes, fasting is not infrequently accompanied by a rapid increase of acidosis and some form of nourishment must be given. Under these conditions, diet is determined by two considerations:

A. Fats are direct precursors of the ketone bodies and hence are contra-indicated.

B. Carbohydrates, under these conditions, are being scantily used by the body and, therefore, if given, elevate the blood-sugar and induce acidosis. This leaves only protein for food which may be used in the form of lean meat and egg, with small amounts of green vegetables as a relish.

The food intake should not exceed three hundred calories daily. The use of alkalis in acidosis is general, but the effect is too often disappointing. Thirty to forty-five grains an hour should be given until the  $\text{CO}_2$  content of the blood is raised to a safe margin. A copious fluid intake and active catharsis are very important, as in uremia.

**Tetanus.** Again the literature contains numerous clinical reports that fully confirm the war experience with tetanus antitoxin, reviewed at length last year.<sup>49</sup> Its efficacy as a prophylactic measure is now undisputed. Its protection would seem to bear a direct relation to the time intervening between the introduction of the organisms into the tissue and the administration of the antitetanic serum. The increased dosage of 1500 units suggested by Tizzoni<sup>50</sup> is now generally employed in preference to the smaller dose of 500 units, as was used in the British army.<sup>51</sup> The necessity of repeated injections is also generally accepted, and it is administered every seven (7) days as long as the wound contains devitalized tissues. The reports of the laboratory work based upon the

<sup>49</sup> PROGRESSIVE MEDICINE, December, 1919, p. 228.

<sup>50</sup> Journal of the American Medical Association, September 14, 1919, No. 2, vol. lxxi.

<sup>51</sup> War Medicine, December, 1919.



vast clinical material supplied by the war, has appeared this year and fully confirms the earlier reports of clinical experience.

The *Report of the Bacteriological Investigation of Tetanus*, carried out in behalf of the war office committee for the study of tetanus and edited by Tullock,<sup>52</sup> is a summary of the scientific investigation of this infection under conditions which have never before been provided. The result is worthy of the opportunity, and this report cannot but be considered a classic. It consists of:

1. An inquiry into the occurrence of the various types of the bacillus tetani in the wounds of men suffering from tetanus.

2. An inquiry into the occurrence of bacillus tetani in wounds of men showing no evidence of tetanus.

3. A discussion of the facts set forth in sections 1 and 2.

4. Experiments carried out *in vitro* to determine whether immune sera, prepared by inoculation of whole cultures into animals, contains antibodies, other than agglutinins, specific to the "types."

5. Experiments conducted *in vivo* to examine the problem of infection with bacillus tetani, as contrasted with intoxication due to absorption of the products of that organism.

The points dealt with in Section 5 are:

- (a) The importance of a suitable nidus for the development of infection.

- (b) Relation with which the degree and nature of the tissue destruction necessary for infection bears to the development of tetanus, and to prophylaxis by antitoxin.

- (c) The part played by concomitant infection with microorganisms other than *Bacillus tetani* in activating or depressing the infective process and the intoxication in tetanus.

- (d) The immunity conferred by the use of mono-typical antitoxic and antibacterial sera.

6. The effect of various dressings upon the growth of anaërobic flora in wounds.

Throughout each phase of the investigation, one object only has been kept in view—the possible application of laboratory findings to the improvement of prophylaxis and therapeutics of tetanus.

1. Tulloch,<sup>53</sup> in 1917, first published his report of the classification of four distinct serological "types" of *Bacillus tetani* and it is interesting to find, after an examination of one hundred cultures of *Bacillus tetani* obtained from wounds of men suffering from tetanus showed: (1) That the value of serum prophylaxis is very great indeed. Practically all the cases of the disease which occur in men who have not received serum prophylaxis terminate fatally. (2) There are indications that, from the higher death-rate, and the early onset of disease among men who did not receive serum prophylaxis, either "types" 2 and 3 are more virulent for man than is type 1, or, the protection afforded by the serum at present in use, is more adequate against infection due to type 1 bacilli than to types 2 or 3.

<sup>52</sup> Journal of Hygiene, August, 1919, No. 2, vol. xviii.

<sup>53</sup> Journal of the Royal Army Medical Corps, December, 1917.

The type 1 bacilli are of more frequent occurrence in nature than are types 2 and 3.

He concludes that the serum at present in use for prophylaxis affords more adequate protection against type 1 infection than against infection with the other types.

2. As a matter of scientific interest, if not of practical importance, a record was kept of the districts in France where each man received his injury. The results suggest at least that the various serological types may have different geographical distribution in view of the relatively large number of type 2 bacilli which were obtained from Flanders. This was further borne out by the fact that during the period of the Flanders offensive, type 2 were frequently found, while with the alteration of the fighting to the Somme area, types 1 and 3 were those commonly obtained.

4. It was found (a) that antitoxic sera do not stimulate phagocytosis of tetanus bacilli; (b) antibacterial sera, prepared by inoculation of whole culture, markedly stimulate phagocytosis; and the relationship between serum and organism is specific to the serological types; (c) tetanus toxin is apparently leukotoxic, but all specimens of toxin are not equally leukotoxic; (d) this leukotoxic factor can be neutralized by antitoxin and the experiment suggests that the neutralization, by anti-toxin, of this leukotoxic factor in toxin is specific in relation to the bacillary types.

5 a-b. Their experiments seem to justify the conclusion: (a) The genesis of tetanus infection induced by experimental methods depends very largely upon the degree and extent of the tissue debility produced by the *inoculum*. (b) The nature of the tissue debilitant employed for setting up infection is an important factor in this connection; for a debilitant which lights up an infection in one animal species may fail to do so in another. Thus, when mice are inoculated with mixtures of saponin and tetanus spores, these animals only occasionally develop the disease. On the contrary, when guinea-pigs are inoculated with such mixtures, they seldom survive, the onset of the disease being usually early and its character fulminant. (c) The quality of the tissue debility induced is also of paramount importance in the genesis of infection. Thus, trimethylamine, even though it is used in sufficient concentration to cause the development of large escars at the site of inoculation, when injected together with tetanus spores into mice only frequently lights up the disease, whereas the toxin of *Bacillus welchii*, injected in sublethal dose together with the same spores, almost invariably sets up tetanus in these animals, notwithstanding the fact that no obvious lesion could be demonstrated antemortem. In animals protected by antitoxin, a rapidly fatal tetanus infection can be induced, provided the spore-contained inoculum produces a sufficient degree of tissue debility of the requisite character. It was shown that in guinea-pigs the onset of the disease can be delayed and its course rendered less acute by increasing the dose of the antitoxic serum; if the increase of the prophylactic dose is sufficient, antitoxin serum may completely protect these animals against an infection induced by inoculation.

5 c. 1. The spasm-producing toxin of *Bacillus tetani*, when employed

in sublethal doses, does not produce sufficient local devitalization of tissue to permit of the growth of *Bacillus tetani* when inoculated along with it.

2. The toxin of *Bacillus welchii* and to a less extent that of *Vibrio septique*, when used in sublethal doses, do produce sufficient devitalization of tissue to allow of the development of tetanus infection. Antitoxins to the products of these organisms protect animals against infection with *Bacillus tetani* when such products are used as tissue debilitants.

3. The protection afforded by tetanus antitoxin can only be partial, for, if the degree of tissue devitalization be great, antitoxin used prophylactically fails to prevent the occurrence of tetanus.

4. Thus the nature of the substance used for producing devitalization of tissue exerts a profound influence upon the development of tetanus spores in the tissues. In guinea-pigs, saponin produces a lesion which always results in the development of spores of *Bacillus tetani* inoculated along with it. The same reagent fails to initiate tetanus infection in the mouse. Trimethylamine, although it may cause the production of a large slough in mice, infrequently causes the development of spores of *Bacillus tetani* inoculated along with it. Calcium chloride of such concentration that it produces no obvious local lesion will almost invariably cause tetanus spores to develop in these animals. Just as the products of *Bacillus welchii* and *Vibrio septique* induce tetanus infection, so certain other relationships, the nature of which is at present not determined, appear to depress the infectivity, or toxigenicity, of certain strains of *Bacillus tetani*.

5 *d*. The experiments described in this section suggest, but do not prove, that while monovalent antitoxic sera exert no specific neutralizing influence on the spasm-producing toxins of any one type, they may nevertheless exert a specific anti-infective influence. This anti-infective influence is quantitative, but not qualitative in character.

The results so far obtained in the investigation of the relative value of antitoxic and antibacterial sera are equivocal. They suggest, however, that this is worthy of more extended investigation. This cannot be done until larger quantities of specific sera are available.

6. The results obtained in investigating the influence which various dressings exert upon the anaërobic flora of wounds, shows that the dressings, which they were in a position to investigate, exerted but little influence.

One important fact emerged from the investigation, namely, that excision of the wound area, irrespective of the dressings employed in the treatment, exerts a beneficial influence. Anaërobe infection is relatively less when this procedure is employed, and convalescence is established at an earlier date than when other methods have been used.

In connection with this work, experiments were undertaken to determine the antiseptic value of certain of the aniline dyes. It is found that their antiseptic activity may be greatly reduced in the presence of fresh tissue, although their activity may not be reduced in the presence of serum.



Tetanus bacilli may be found in wounds at any time during the process of healing. In one instance *Bacillus tetani* was recovered from a wound eight hundred and eighty-two days after the infliction of the injury. It is sometimes difficult to demonstrate the presence of *Bacillus tetani* in such circumstances, and several swabs may have to be taken before their presence is appreciated by the observer.

Its value as a therapeutic measure is still doubtful, and they support the statement of Bruce<sup>54</sup> that there does not seem to be any statistical evidence that serum given therapeutically has any marked effect upon the rate of mortality. The experimental work of Keel and Emberton, suggests, however, the lines along which rational therapy may be developed.

*The paths of spread of bacterial exotoxins with special reference to the tetanus toxin.*<sup>55</sup>

In 1903, Meyer and Ransome<sup>56</sup> concluded from their experiments that tetanus toxin reaches the central nervous system solely by way of the axis cylinders of the motor nerves, and that if it ascends by the sensory nerve toward the cord, the posterior root ganglion acts as a block to further spread, since tetanus dolorosus only develops when a poison is experimentally inoculated into the posterior root between the ganglion and the cord. They came to the conclusion that the toxin did not spread to the cord by way of the perineural lymphatic sheaths. Orr and Rows,<sup>57</sup> however, showed that if bacteria were left in contact with the nerve trunk they could be demonstrated in the spinal cord, having traveled along the perineural lymphatic sheaths of the posterior root to the cord. Teale and Emberton conclude in their experiments:

1. That although tetanus toxin ascends to the central nervous system by way of the axis cylinder of the nerves, it also, to a very great extent, passes up the nerves to the cord by way of the perineural lymphatics. Blocking of the latter path greatly delays, and in some cases completely prevents, the occurrence of tetanus in the part corresponding to the nerves whose lymph path has been blocked.

2. Although tetanus toxin passes rapidly from the bloodvessels into the connective tissue spaces, and thence to the thoracic duct, the toxin does not pass from the capillaries of the central nervous system to the tissues thereof.

3. Tetanus antitoxin does not pass to the central nervous system either by the way of the bloodvessels, axis cylinders, or neural lymphatic channels. It also cannot pass from the cerebrospinal fluid, when injected intrathecally, into the substance of the cord. The antitoxin simply acts by combining with the circulating toxin at the seat of production, and prevents it from reaching the central nervous system. The toxin which has already reached the central system is unaffected by antitoxin.

<sup>54</sup> War Medicine, December, 1919.

<sup>55</sup> Journal of Pathology and Bacteriology, Cambridge, October, 1919, No. 1, vol. lxxxiii.

<sup>56</sup> Arch. f. exper. Path. u. Pharmakol., Leipzig, 1903, lxix, 367.

<sup>57</sup> Edinburgh Medical Journal, 1916, xvii, 78-89.

**Anesthesia.**—The year's literature is almost unanimous in the support of Blake's statement quoted last year "that as a result of our war experiences it is probable that nitrous oxide with oxygen will be employed in the future to the exclusion of the other general anesthetics, except ether, which will be used as an adjuvant." That these clinical experiences have already been confirmed by experimental observations is shown by the work of Reimann and Bloom at the Lankenau Hospital. They not only found the alkaline reserve of the plasma to be diminished in every case in which any of the alcohol group of anesthetics were employed, ether, chloroform and ethyl chloride, but that when nitrous oxide-oxygen anesthesia was used, there was no change in the alkaline reserve, and it was possible, with the artificial supply of oxygen given, to maintain the oxygen content of the blood at, or above, normal, and thus prevent superimposing the acidosis of anesthesia upon that caused by other factors of the disease or the operation itself.

Dale<sup>58</sup> has been able to furnish further experimental confirmation of the increased danger in the use of the alcohol anesthetics over nitrous oxide and oxygen. He has previously established the possibility of producing a shock-like state with the chemical histamine, a substance which is similar to, if not actually the same as, the chemical products obtained from dead and devitalized tissues. By injecting constant quantities of this shock-producing substance into a series of animals and then anesthetizing them with chloroform, ether and nitrous oxide and oxygen, he was able to demonstrate constantly that the greatest degree of shock would follow the use of chloroform, next ether and the minimum degree always when nitrous oxide and oxygen were employed. Dale feels that it is probable that the normal resistance of healthy subjects to the products of devitalized tissues can be assumed to be more or less alike, and that in this series of experiments it was demonstrated that chloroform and ether in some way depress or embarrass this normal resistance to a far greater degree than nitrous oxide and oxygen. That our overwhelming clinical experience of the last few years can thus be confirmed by such careful experimental research is indeed encouraging and will probably deter, and at least inhibit, surgeons in deciding upon the choice of an anesthetic from their limited personal experience. Dale further suggests that the greater safety in civil surgery of a combination of local anesthesia with nitrous oxide and oxygen (the anociation of Crile) as compared with prolonged anesthesia with ether or chloroform may find its true explanation along these lines rather than exhaustion of the nerve cells of the central nervous system. It at least broadens, the significance of the chemical factor in shock, and further research in this direction should prove very valuable.

**THE USE OF ALKALOIDS IN COMBINATION WITH GENERAL ANESTHETICS.** Barton says<sup>59</sup> alkaloids have been used as a preliminary to the administration of anesthetics for some years, and there is a general, almost unanimous, opinion among anesthetists as to their value, while among surgeons there is still some diversity of view. He feels that the main object is to contribute to the safety and comfort of the patient. With

<sup>58</sup> British Journal of Experimental Pathology, April, 1920, i, 103.

<sup>59</sup> Practitioner, 1919, ciii, 253.



them many operations can be done under an extremely light narcosis which otherwise might have called for a deep ether anesthesia. The patient, therefore, while on the table is in a condition of safety, and, because of the small amount of anesthetic employed, has less unpleasant postanesthetic vomiting and is certainly free from the risks of acidosis and ether bronchitis. The other advantages are greater calmness and placidity, since the operation has lost its terrors for him because of his drowsiness; the mucous membranes are dry and the hypersecretion of mucus, so common with ether anesthesia, is usually absent.

In some cases, however, certain individuals have an idiosyncrasy for morphine and there is excitement instead of drowsiness, nausea and vomiting, headache and constipation. If this is known beforehand, morphine should be avoided, otherwise it is well to go on the principle of "the greatest good to the greatest number." Morphine, grain  $\frac{1}{4}$ , and atropine sulphate, grains  $\frac{1}{100}$ , are the alkaloids he usually employs. Morphine is the principal factor in causing the drowsiness and placidity, and has some drying influence on the mucous membranes. Atropine has little or no narcotic effect, and on occasions acts as an excitement; During the anesthesia, the effect of morphine on the respiratory center must always be borne in mind. It is a depressant, reducing the frequency and depth of respiration. Ether, on the other hand, is a respiratory stimulant, and the result of the combination is to produce a regular type of breathing, as a rule a little quicker and deeper than natural, but not the type associated with ether alone. He warns, when using alkaloids, against producing a deep narcosis of the third stage, the so-called surgical anesthesia. So long as the patient suffers no pain and the operator is not embarrassed by reflex movements, all requirements are satisfied.

The effect of alkaloids on the pupil are fairly constant and will not embarrass the anesthetist when once he is familiar with them. Morphine, whether accompanied by atropine or not, contracts the pupil. The degree of contraction is an index of the effect of the morphine on the patient, and, if it is pronounced, the patient will require very little anesthetic. The contracted morphine pupil persists throughout the anesthesia and does not follow the usual stages. A moderately contracted pupil, reacting sluggishly to light before the anesthetic and not at all during its administration, is the best and most common in a combined morphine and ether anesthesia. The reflexes during these mixed narcoses are sometimes very brisk. The corneal reflex is especially so, and, in fact, he never tries to abolish it.

The effect of morphine on the stage of recovery is to prolong it. The patient may, or may not, have a preliminary vomit on the completion of the operation and before returning to consciousness. In any case, he generally dozes comfortably for some hours after, a decided advantage. The best time to administer alkaloids is one hour before that fixed for operation. After a prolonged experience in hospitals, he feels that the effects of the alkaloids is at about its height between one and two hours after administration; on the other hand, they do not, as a rule, develop their action within less than half an hour.

**CHLOROFORM ANESTHESIA.** It is interesting to see the gradual change of opinion of English anesthetists in their feeling about chloroform.



Silk<sup>60</sup> states that the routine use of chloroform is to be discouraged, for even in the hands of the most skilled the mortality is high and closely approaches 1 in 2000 cases. More ether is being used in the English hospitals now than twelve months ago, and definitely good results have followed the change, for the death-rate for the quarter ending September 30, 1919, was less than one-half of the average of the preceeding two quarters. He credits this change to the influence of the American anesthetists and surgeons during their association with the English in the war.

N. C. Davis<sup>61</sup> demonstrated experimentally that starved animals are very susceptible to the uniform liver injury tha tresults from chloroform. As might be expected, a maximal injury follows when animals are in a state of starvation.

When sugar and diets rich in carbohydrates are fed in the days preceding chloroform anesthesia, they have a marked protective action against liver injury.

Fat alone, or combinations of food containing fat in large proportions, induce a maximal susceptibility to liver injury which is comparable to that induced by starvation. Beef extract is highly protective in proportion to its actual food value. The skeletal muscle and heart muscle have but a slightly protective action. The liver and kidney exert a considerable protection. Brain, although rich in lipid substances, is a protective food against chloroform injury, thus being very unlike the usual fat mixtures. Skim milk alone and commercial casein alone, or in combination with cracker meal, are highly protective diet.

No single theory so far advanced will explain this peculiar protective action of certain food substances against the liver injury of chloroform anesthesia. The practical significance of this work, of course, is that patients to whom chloroform is to be given [if it is ever justifiable], should receive liberal amounts of carbohydrates and skim milk for at least two days preceding the anesthesia, and it cannot be too often emphasized that it is dangerous to give chloroform to man or animals whenever a fasting period has preceded the administration of the anesthetic.

**ANALGESIA.** There is an incipient analgesic condition in the early stages of every inhalation narcosis. When ether is given this analgesia is obtained after ten to twenty inhalations and, under its influence, many minor operations can be painlessly performed. Traddei<sup>62</sup> prefers to designate this short analgesia as psychic block, as he believes it is not due to the chemical action of ether on nerve centers but is analogous to the well-known analgesia observed in great emotion.

**ETHER-OIL COLONIC ANESTHESIA.** Lathrop<sup>63</sup> reports the experience of ether-oil colonic anesthesia in 1002 cases.

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<sup>60</sup> American Journal of Surgery, 1920, vol. xxxiv, Anesthesia Supplement No. 2.

<sup>61</sup> Archives of Internal Medicine, 1919, xxiii, 612.

<sup>62</sup> Riforma Med., 1919, xxxv, 896.

<sup>63</sup> Journal of the American Medical Association, July 10, 1920, No. 2, vol. lxxv, 82.

He first emphasizes that the mixture should only be used by one who can begin its administration and have it under his care throughout all the cases. It should never be delegated to a different physician or nurse each time it is used. The patient should be under observation for twenty-four hours or more. The evening before operation an enema of soap suds (two pints) is given. A second enema of one or two pints of clear, tepid water is given early the next morning. If the operation is scheduled for 11 A.M., then at 9.30, 2 drams of olive oil (warm), 3 drams of paraldehyde and 4 drams of ether, are introduced into the rectum and lower bowel. The patient should be kept as quiet as possible. At 9.50 A.M.,  $\frac{1}{4}$  grain of morphine and  $\frac{1}{150}$  grain of atropine are given hyperdermically. At 10.20 A.M., 3 or 4 ounces of ether and 2 ounces of olive oil (warm) are introduced into the rectum and lower bowel. The oil and the ether are put into a bottle and shaken thoroughly. With the patient lying on the left side and both knees flexed, the right acutely, the solution is introduced by means of a rectal tube and funnel. The tube is introduced about six inches. The injection should be given slowly, about 1 ounce a minute, the funnel being held about 3 inches above the level of the patient. The tube should be clamped and allowed to remain in the rectum so that the mixture may be withdrawn during the operation if there should be any indication for doing so. After the rectal injection, the mouth and nose of the patient should be covered with several thicknesses of gauze. If the patient cannot retain the ether-oil mixture, one should not try to repeat it but should abandon the method. The patient should be ready for operation in from twenty to thirty minutes from the time the last injection is given. The reversed Trendelenburg position seems to aid in maintaining an even plane of anesthesia. The jaws should be supported so that respiration will be unobstructed.

When the operation is completed, the bowel should be well irrigated with tepid water until it returns clear. The colon may be gently massaged from right to left to aid in its evacuation. One pint of water is then put into the bowel or olive oil given in the quantity of 4 ounces to prevent any possible irritation. In their 1000 cases only two instances of irritation occurred.

In their experience it finds its greatest application in hyperthyroidism or exophthalmia. It is contra-indicated in rectal disease or when pain is caused by its introduction. It is not recommended for routine use, as the time required for successful administration would not permit of this method when a number of operations were scheduled.

Gwathmey, in a discussion of the paper, emphasized the following principles:

1. Ether-oil colonic anesthesia is one of the easiest methods to administer, requiring only a rectal tube with attached funnel.

2. It is one of the safest methods. The margin between full surgical anesthesia and a toxic dose is greater than with any inhalation method.

3. It is one of the most pleasant methods for the patient as attested by the fact that those who have tried other methods prefer the colonic.

4. A greater relaxation of the musculature exists than is usual with any inhalation anesthetic.

5. A smaller amount of ether per hour is required than by any other method. The estimated amount is two ounces per hour which seldom varies.

6. It is regulated as easily as any inhalation method by: (a) Covering the face with a towel to deepen the anesthesia, (b) by placing an airway tube in the mouth to lighten the anesthesia or (c) by unclamping the rectal tube and draining the residue and flushing thoroughly to remove the contents of the rectum. Gwathmey says that it can be terminated at any time as far as the anesthetic is concerned, the patient continuing to sleep from the other drugs used.

Horsley feels that because of the fact that the ether is carried through the portal circulation on its way to the general circulation that in the exophthalmic goiter cases unfortunate results may follow because of the already crippled condition of the liver. It is like giving ether by inhalation to a patient with seriously damaged lungs.

As to the claim that the anesthesia can be terminated at any time we feel that it needs some qualification. In the cases in which Gwathmey used it, in some of the base hospitals abroad, surgeons did not feel that it was as safe as inhalation anesthesia, particularly nitrous oxide and oxygen, and chiefly because of the effects persisting for some time after the ether-oil mixture had been removed from the bowel. Theoretically, this is what one would expect from a liver and general circulation surcharged with ether.

**RECTAL ANESTHESIA.** Manine and LePage<sup>64</sup> believed from their experience that rectal anesthesia is dangerous only if doses greater than from 60 to 100 c.c. are used. They have used pure ether rather than ether mixed with oil and have never obtained irritation of the rectal mucosa. Anesthesia is complete at the end of twenty or thirty minutes but the awakening is slow, from one and a half to two and a half hours after the beginning of the anesthesia.

Vitraz,<sup>65</sup> in a series of 67 cases in which he used ether oil, had anything but satisfactory results. Sleep was perfect in only four-tenths of the cases, imperfect in five-tenths. It was followed in a few hours by vomiting or abdominal pain, and in several instances pulmonary and hemorrhagic gastro-intestinal complications followed. There was one death. He collected reports of 2500 cases, in which there were 8 deaths and 8 cases of severe complications, from which it certainly would seem that it is more dangerous than any other form of anesthesia at present in use, and he feels that as now practised must be classed as unquestionably dangerous and its use should be discontinued.

**LOCAL ANESTHESIA.** The report of the Committee on the Advantages and Disadvantages<sup>66</sup> of the various local anesthetics in nose and throat work has, in some of its aspects, a bearing upon its use in general surgery. Quinine and urea hydrochloride, the only local anesthetic that produces edema and sloughing, has been practically abandoned in this field of surgery and also in general surgery. Crile and Lower<sup>67</sup> still advocate

<sup>64</sup> Arch. de Pharm., March, 1920, cvii, 284.

<sup>65</sup> Bull. et mém. Soc. de chir. de Paris, 1919, xiv, 934.

<sup>66</sup> Journal of the American Medical Association, July 31, 1920, No. 5, vol. lxxv.

<sup>67</sup> Surgical Shock, Philadelphia, 1920.



its use in massive infiltration of the abdominal wall *at a distance from the incision*. Their object is to insure a lasting effect of the anesthetic, quinine and urea lasts for two or more days and, they feel, minimizes the postoperative shock. They emphasize, however, that it is used only in cases which are grave risks.

In the committee's investigation of the toxic effects of local anesthetics, they speak of mild, grave, threatening, and sudden death. Recent literature contains the record of 2 deaths from cocaine, 3 deaths from procaine, 1 death from apothecin. Several deaths or poisonings were recorded following the use of beta-eucain. As a result of a questionnaire to the members of the section, there were 14 deaths reported following the use of cocain, and 6 deaths following the use of procaine in nose and throat operations. Of the cocaine deaths, 5 were due to avoidable mistakes, such as overdose. The remainder died within a very short time, usually within three minutes after the administration of the drug. As some of these cases have already been recorded, there is no means at hand of ascertaining the proportion of deaths occurring as compared to the number of cases in which the local anesthetic was used. They do not, as a result of their review of the recent pharmacologic studies of the various synthetic preparations used for local anesthesia, advise against the preliminary administration of morphine, but rather encourage its continued trial. They feel that the ideal anesthetic having the effects of cocaine, and yet being absolutely non-toxic, has not been found.

#### Summary:

1. There is a remarkable similarity in the clinical effects and animal experimentation with the synthetic preparations used for local anesthesia.

2. None of the synthetic products equals cocain in its local effect when applied to the mucous membrane.

3. These synthetic products may be freely injected, if slowly done, in proper doses in unlimited quantities.

4. Fatalities occur either immediately or not at all.

5. The drugs are eliminated by the liver.

6. The greatest danger lies in too rapid injection or entering a vein. Matas<sup>68</sup> in discussing the report emphasizes the value of morphine given one-half to three quarters of an hour before the anesthesia is begun, and the value of combining epinephrin with the drug used for the local anesthesia. Local anesthesia is to be used where there is quiet; when the patient is properly prepared; where there are no distracting noises; and where the proper man can do his work in the proper clinic. For that reason it will never entirely supercede general anesthesia. Then there are persons who are psychically unfit for local anesthesia, who are sympathetic, who are in a constant state of agitation.

*Blocking the Splanchnic Nerves.* Preiss and Ritter,<sup>69</sup> report 89 cases in which the splanchnic nerve was blocked from the rear. It is reached from just below the twelfth rib, at a depth of approximately 7 cm.

<sup>68</sup> Journal of the American Medical Association, July 31, 1920, No. 5, vol. lxxv.

<sup>69</sup> Zentralbl. f. Chir., Leipzig, December 13, 1919.

above the second lumbar transverse process, by introducing the needle at the lateral convex margin of the vertebra, and depositing from 10 to 40 c.c. of a 1 per cent. procain—epinephrin solution. The patient may be prepared with a sedative the evening before and again half an hour before the operation. In only 4 of the 89 cases was it necessary to supplement the nerve blocking with inhalation anesthesia. Cancer involving the nerves was responsible for failure in 2 of these cases; phlegmonous appendicitis in another; the fourth was an ovariectomy; blocking the splanchnic nerve does not anesthetize the ovaries. Fifteen different types of operation were performed, gastric, abdominal and renal. The youngest patient was eleven, the oldest seventy. No serious after-effects were noted. The special field for splanchnic anesthesia is for major operations on all organs of the greater abdominal cavity and for interventions for severe acute peritonitis, as after perforation of a viscus.

*Benzyl Corbonal.* The substitutes for cocaine have usually been constructed on the benzoic acid nucleus esters. Macht discovered that benzyl alcohol manifested anesthetic powers and that this action was probably due to the benzyl grouping. Hjort and Egan,<sup>70</sup> as a result of their study of the anesthetic properties of another benzyl grouping, have found that *benzyl carbonal*, which is pure oil of rose, possesses local anesthetic properties which, from laboratory studies, seem to be superior to those of benzyl alcohol. The toxicity of rose oil, as determined on white mice and a dog, is about the same as that reported by Macht for benzyl alcohol. However, it is more stable than benzyl alcohol which is a distinct point in its favor. The solubility of rose oil is sufficient for its anesthetic use.

*The Pharmacology of Local Anesthetics.* Eggleston and Hatcher<sup>71</sup> find that the most important result of their investigation is that the essential elimination of all the local anesthetics studied, except cocaine and holocaine, proceeds with great rapidity and is completed within a few minutes following the intravenous injection of a lethal dose. The essential elimination of cocaine and holocaine is a much slower process, and cocaine may not be completely eliminated for two or more days. In the cat, local anesthetics are destroyed in the liver, and it is highly probable that man eliminates these drugs in the same way.

Local anesthetics can be divided into two groups according to their rate of elimination: Group one including those which are rapidly eliminated, such as alypin, apothetin, betaeucaine, nirvanin, procaine, stovaine, and tropacocaine. Group two includes cocaine and holocaine, which are very slowly eliminated. This explains the relatively low toxicity of the members of the group one.

**SPINAL ANESTHESIA.** Wells,<sup>72</sup> from his experience with Delmas during the late war, reports upon the use of anhydrous cocaine in spinal anesthesia. He sums up the advantages of spinal anesthesia as follows: (1) Perfect analgesia. (2) Perfect muscular relaxation. (3) Absence

<sup>70</sup> Journal of Pharmacology and Experimental Therapeutics, 1920, xxiv, 211.

<sup>71</sup> Journal of Pharmacology and Experimental Therapy, 1919, xiii, 433.

<sup>72</sup> Annals of Surgery, April, 1920, No. 4, lxi, 504.



of postoperative shock. (4) Absence of postoperative gastric disturbance. (5) Absence of postoperative motor restlessness, so often difficult to control in ether narcosis. (6) Retention of consciousness, thus allowing of a deciding point, as, for example, removal of two ovaries instead of one, as intended, also allowing of drug administration of the mouth, coffee, etc. (7) Immediate resumption of gastro-intestinal activity if operative conditions permit. To these he adds the operative advantages of extreme ease of retraction of the muscles. The lessened tendency of the intestines to crowd the operative field. The relief in spastic or paralytic ileus, at times even removing the necessity for operation (Babcock reports several cases of this kind). The saving of one pair of hands for other purposes during the operation.

The *disadvantages*: (1) The retention of consciousness is often a disadvantage, for example, in a highly neurotic individual. (2) Manipulation of the stomach and the intestines sometimes gives rise to a sinking sensation and unpleasant psychic disturbances which are, however, rarely dangerous to life. (3) After a fixed amount of the analgesic agent has been injected, it cannot be removed nor can its effect be controlled. (4) It cannot be as easily obtained nor is the technic of its administration so simple as ether anesthesia. (5) Failure of anesthesia is reported in from 4 to 9 per cent. of cases.

The *indications* and *contra-indications* are as follows: Spinal analgesia is *indicated* in: (1) Cardiac conditions, alone or with broken compensation. (2) Renal conditions, especially in the presence of impending uremia. (3) Pulmonary conditions other than (a) acute febrile tuberculosis; (b) large pulmonary effusions; (c) large intra-thoracic growths. (4) Inguinal, femoral and ventral hernias. (5) Shock, if blood pressure is not too low or falling, especially in railroad accidents to the leg or pelvis, and in severe burns or scalds. (This is usually considered by surgeons as a distinct contra-indication to spinal anesthesia. A personal experience with war injuries resulted in a final abandoning of spinal anesthesia in cases of shock. It is true that we were employing stovaine, and the anhydrous cocaine of Delmas may have a different physiological action.) (6) Acute abdominal conditions, including appendicitis with, or without, peritonitis, intestinal obstruction, and paralytic obstruction. (7) Reduction of dislocations. (8) Operations on the anal region, urethra, bladder, prostate, uterus, and appendages. (9) Plethora, atheroma, and chronic alcoholics. (10) Where an acute operation is imperative a short time after the ingestion of a full meal.

Of the *contra-indications*, he mentions: (1) Lowered blood-pressure (hypotension). (2) Turbid spinal fluid. (3) Diseases or tumors of the brain, cord, and meninges. (4) Recent syphilis. (5) Intrathoracic conditions as (a) large effusions; (b) large growths, mediastinal especially. (6) Advanced toxic or moribund cases of peritonitis. (7) Acute febrile infections, especially acute pulmonary tuberculosis. (8) General sepsis or separation near the point of spinal puncture. (9) Where the patient cannot stay in bed for at least twenty-four hours after operation.

This seems to be a fair presentation of the advantages and disadvantages, indications and contra-indications of spinal anesthesia at the



present time, probably a little too enthusiastic. He reviews the various agents which have been and are being used and calls attention to the preparation of cocaine evolved by Delmas of the University of Montpellier, France. Delmas practically applied the technic first suggested by Le Filliatre in which various levels of anesthesia were obtained by controlling the diffusion of the drug by elevation of the spine and varying the size of the dose. Delmas' experience with the procedure led him to modify the technic so as to attain unity of dose with unity of time, whatever might be the height desired:

*Instrumentation.* The spinal puncture needle is of the trocar and cannula type, the needle preferably of platinum-iridium, 7 cm. long, 1.4 mm. diameter, and the point of it preferably of an abrupt bevel. The syringe is an all glass Luer of 20 c.c. capacity.

*Anesthetic Agent.* A purified hydrochlorate of cocaine prepared by a special process which will be described later. This cocaine is in a crystallized form, dry, and should be in sterile ampoules, and dissolved at the moment of its use in the cerebrospinal fluid of the patient. Solutions prepared in advance, by reason of the molecular action observed, renders them promptly unreliable and injurious, sterilization acts in the same way, heat altering the physiologic activity of the product.

The lumbar puncture is performed between the fourth and fifth lumbar vertebræ. The syringe takes in 20 to 25 c.c. of the spinal fluid, when it is detached from the needle and the trocar inserted. Twenty cubic centimeters of the spinal fluid are thrown away and to the required dose of dry crystals of cocaine (.01 to .05 gm.) is added the remaining 5 c.c. of the spinal fluid. This mixture is gently agitated in the ampoule until there is a perfect solution when it is sucked into the glass syringe and then, after the removal of the trocar, the syringe is reattached to the spinal needle and 20 c.c. more of spinal fluid is drawn into the syringe, when the whole is thrown forcibly back into the subarachnoid space. The force used is in proportion to the height of anesthesia desired (the higher the level of the anesthesia the more force necessary). This column of analgesic liquid immediately diffuses in a homogenous fashion into the remaining spinal fluid which impregnates to the same degree all the posterior roots of the spinal nerves. The reason for this is that to the preliminary hypotension created by the removing of 20 c.c. of spinal fluid there is added the force of penetration of a relatively large charged mass (over one-third of the spinal fluid which has remained in the subarachnoid space).

The analgesia of the entire body is instantaneous if a maximum force is used. The sensation of contact and temperature are not necessarily disturbed, only conduction of pain is totally interrupted independent of the elevation of the spine. The quality of the analgesia is not altered by the size of the dose of the agent, it is simply the duration, .01 gm. produces the same result for fifteen minutes as .04 gm. does for one and one-half hours.

Delmas reports, in his 431 cases, no failures, no mortality.

The method of purifying the cocaine has been developed by Professor Gardin. It consists in dissolving a given quantity of commercial hydro-

chlorate of cocaine in a given amount of absolute alcohol, recrystallizing by the addition of absolute, water-free ether (sulphuric); decanting off the liquid, drying the crystals in vacuum or sulphuric chamber. The crystals should be stored in glass ampoules which should be colored brown.

**Wound Treatment.** Time has, to a large extent, settled the controversy over wound treatment. The realization that war wounds differ only from civil wounds in degree and that the etiological factors are the same in both of them was the starting-point of the unraveling of this confusion. The factors in wound infection are now accepted to be (1) the infecting organism; (2) the interval time between the implantation of the organism and its surgical or mechanical removal; (3) the extent and degree of devitalization of the tissues resulting from the injury; (4) the promptness and thoroughness with which these devitalized tissues are removed from the wound; (5) the promptness and completeness with which the wound, after it has reached the stage of surgical sterility is closed and covered with skin.

1. The *character of the infecting organism* has been shown, by war experience, to have perhaps the greatest influence upon the future course of the infection. The whole theory of surgical sterility, which is not a condition of asepsis by any means, depends upon the principle that well-nourished tissues cannot only withstand, but also eliminate, infection. This principle applies to practically all organisms except the streptococcus, and no one at the present time should attempt to close a wound that contains this organism, for failure is almost certain. Therefore, in the very beginning of the surgical treatment of a traumatic wound, a simple smear should be made from several portions of the wound surface to determine if this organism be present, and, if present, the wound must remain open until it disappears.

2. *Time Interval.* There is a period of from three to eight hours between the implantation of the organism and the development of sufficient growth to penetrate beneath the surface of the wound, varying greatly, of course, in the type of the wound. This is the so-called period of contamination. If the wound is received by the surgeon within this period, and smears do not show the presence of streptococci, and it is possible to remove all devitalized tissues by excision with the scalpel, an effort should be made to close the wound. The deep tissues should be approximated layer by layer by interrupted catgut sutures after perfect hemostasis has been obtained. Then the skin edges are united with silkworm sutures, care being taken to avoid the least bit of tension. If tension is unavoidable, the skin should be freed from the underlying tissues by undercutting or making relaxing sutures in the skin several inches away from the incision and parallel to it. With the first signs of clinical infection, as fever, redness and swelling of the wound, a platinum needle should be inserted and a smear and culture made to again determine if streptococci be present, and if the examination is positive, the wound should be widely opened. In the absence of streptococci it can be watched from day to day, and it is surprising the large proportion of such wounds that will heal without



developing frank suppuration. This is called primary suture and is the ideal treatment of traumatic wounds.

*Delayed primary suture of wounds* is a term applied to suture of a wound which has had to be postponed because of (a) the inability to keep the patient under the same surgeon's care for a period of fifteen days, (b) the presence of streptococci in the wound. This delayed primary suture cannot be safely employed after the fifth day. If the wound has been mechanically cleaned (débridement) at the primary operation, and contains no streptococci, Duval and others claim that the reinfection of the wound will be prevented if it is merely covered with dry sterile gauze.

In our own experience we prefer the application of a 5 per cent. solution of dichloramine-T, the English used flavine very extensively for this type of wound. If the wound contains streptococci, some chemical sterilization should be attempted, dichloramine-T, or Dakin solution. The dyes, such as flavine and malachite green, were not very successful as germicides for streptococci. When the wound has reached surgical sterility it is sutured layer by layer without further excision or freshening of the wound surfaces, and the skin closed as in a primary suture.

*Secondary Suture of Wounds.* It was found possible to treat more than two-thirds of the massive wounds of war by débridement and primary suture and this gives a basis upon which we can estimate the need for mechanical and chemical methods for the débridement and secondary suture of wounds in civil life. In other words, infected traumatic wounds in the vast majority of cases are the result of inadequate provision for immediate treatment by a skilled surgeon. Our efforts in civil life should be directed toward developing such organizations in our hospitals, communities and industrial plants, that every traumatic wound should receive skilled maximum surgical attention within the period of contamination, and if this is provided, primary suture and the prevention of infected traumatic wounds will be assured in far more than the 75 per cent. that was obtained in the war. Delayed primary suture is necessary when (a) the wound is received after the period of contamination and when infection has been established; (b) the presence of streptococci in the wound; (c) the presence of such masses of devitalized tissues or such degree of inflammatory reaction in the surrounding tissues that it is impossible or inadvisable to completely remove it by mechanical débridement; (d) the area or anatomical conditions are such that it is mechanically impossible to close it by suture. In this type of wound, especially where there are large masses of devitalized tissue, the use of Dakin solution by the intermittent instillation method of Dehelley and Carrell is the best treatment we possess at the present time. The Dakin solution is used, not primarily as an antiseptic, as was first supposed, but as a chemical solvent of the dead tissues. With this solution, it is possible to obtain a chemical débridement of the wound in cases in which it would be fatal to the patient to attempt its mechanical removal. In the section on antiseptics, this recent explanation of the chemical action of Dakin fluid is described in detail. It is sufficient here to say that the sodium hypochloride, whose formula is crudely expressed by  $\text{NaOCl}$ , when it



comes in contact with dead tissue gives off the radical Cl which unites with the amine radical of the protein of the wound contents to form chloramines ( $\text{NH}_2\text{Cl}$ ). At the same time, a hydrogen radical is given off from the protein which unites with the NaOH to form a hydroxide. It is the hydroxides thus formed, when sodium hypochlorite comes in contact with dead tissues, that act as chemical solvents of this material. In this chemical reaction the hydroxide, which is formed, is always of the same amount as there is protein chemically available in the dead tissues and as soon as the dead tissues are removed, this formation of hydroxide ceases.

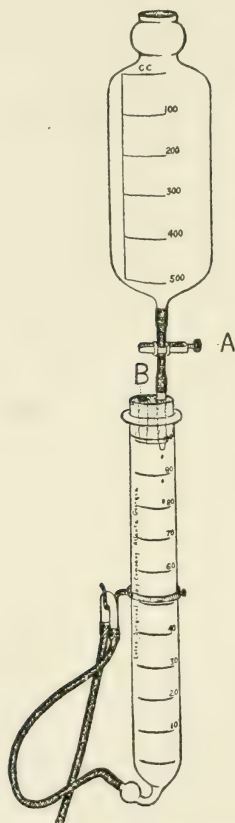


FIG. 45.—Device for intermittent flushing of wounds. (Ballenger and Elder.)

With the removal of the devitalized tissues the bacteria disappear, and when cultures show that the wound has become surgically sterile, every effort should be made to close it by anatomical layers, with a covering of skin, as was described in the primary suture of wounds.

Bowlby<sup>73</sup> concludes his address with these words: "Not only were many lives and limbs saved by primary wound closure, but compound fractures healed more rapidly and with much less necrosis,

<sup>73</sup> Surgery, Gynecology and Obstetrics, January 30, 1920, xxx, 91.

joints were saved from acute arthritis, suppuration of wounds became rare, septic infection with fever and emaciation diminished, and convalescence was infinitely more rapid. He predicts that drainage tubes will be much less employed in the future treatment of wounds, and that primary, or delayed primary, suture will become, in civil life, a common method for the treatment of compound fractures and the lacerated wounds caused by machinery." Anything less than this should not satisfy any surgeon and our own personal experience since returning from overseas is that our hospital patients, many of whom have seen such standards of treatment while in the army, demand this new standard of surgical care of traumatic wounds.

**A Device for the Automatic Intermittent Flushing of Wounds.** Balinger,<sup>74</sup> by means of the device shown in the illustration, provides an automatic intermittent supply of medicated solution, such as is required by the Dakin-Carrel method of treating wounds. It has merely to be connected with an irrigating container and a screw compressor on the tube leading from it so adjusted that a given number of drops flow per minute. When the fluid collects to the level of the tube at *C*, siphonage is established and the solution flows through the exit into the wound. The amount to be delivered may be varied by raising or lowering the tube at *C*, while the frequency of the flushing is regulated by the rate of the drops per minute. In this manner wounds may be flushed with solutions as desired without the aid of a nurse or an attendant. The only thing necessary being to keep the solution in the irrigating container, which may be of sufficient size to last for twenty-four hours. Such a scheme is practical and warrants its installation in a busy surgical ward, for the second hourly attention required of the nurse, or the proper Carrel-Dakin treatment, is difficult to obtain under the present shortage of hospital personnel.

**Tidal Irrigation of Wounds by Means of a Liquid-tight Closure.**—W. H. Taylor and N. B. Taylor,<sup>75</sup> by means of a rubber irrigating cap designed to make a liquid-tight contact with the skin circumferentially about a wound, introduce antiseptic fluid into the wound without leakage even though it be under considerable pressure. The antiseptic fluid is introduced under slight positive pressure until the fluid has permeated every crevice of the wound and this is allowed to remain for about a half hour. This is affected by closing the outflow tube of the apparatus and opening the inflow tube which is connected with a suspended irrigating bottle. After a half hour of positive pressure, suction in the wound is brought about by siphonage, established by closing the inflow tube and opening the outflow tube. This ebb and flow movement of the antiseptic fluid is believed to have a marked cleansing action as regards the wound secretions, while the effect of the negative pressure is to induce hyperemia and lymphorrhea, to increase phagocytosis and to "cause a forced output of bacteria from the wound."

This is an entirely new principle, as far as we are aware, in the treatment of wound cavities. The report is extensive and in detail, and

<sup>74</sup> Journal of the American Medical Association, May 8, 1920, No. 19, lxxiv, 1315.

<sup>75</sup> *Ibid.*, June 19, 1920, No. 25, lxxiv, 1700.

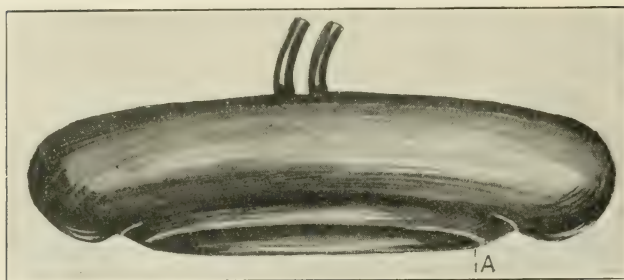


FIG. 46.—Appearance of the appliance, with the inflow and outflow tubes, the loose covering portion of the rubber and the outer aspect of the circumferential valve (A). (Taylor.)

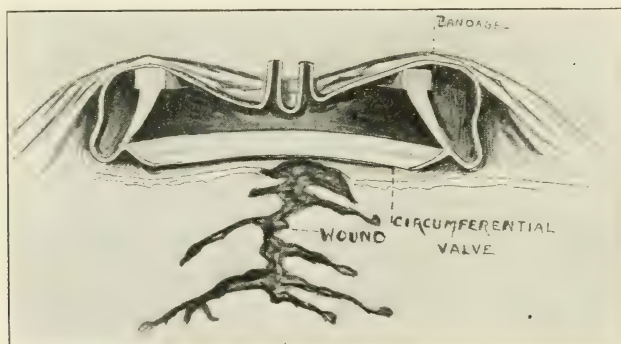


FIG. 47.—Sectional view of a ragged wound covered by the appliance. The rubber is sucked down to the skin surface and the wound is shrunk in by the action of negative pressure. (Taylor.)

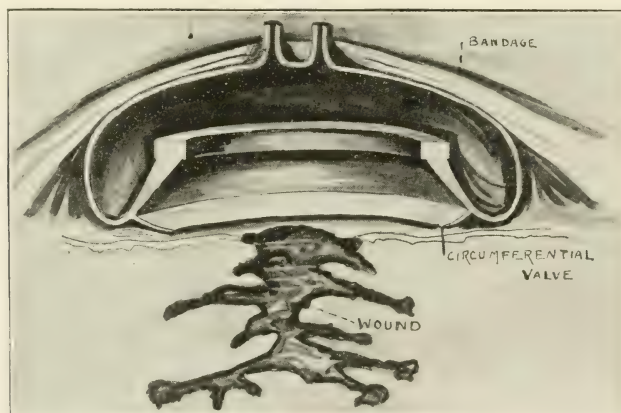


FIG. 48.—Sectional view of the same wound shown in Fig. 2, in which the wound cavity is dilated and the appliance distended, by the action of positive pressure. (Taylor.)



should be read in the original. To those who have labored in the last three or four years with the problem of wound irrigation, this device appeals, from a theoretical standpoint, and it certainly should have a

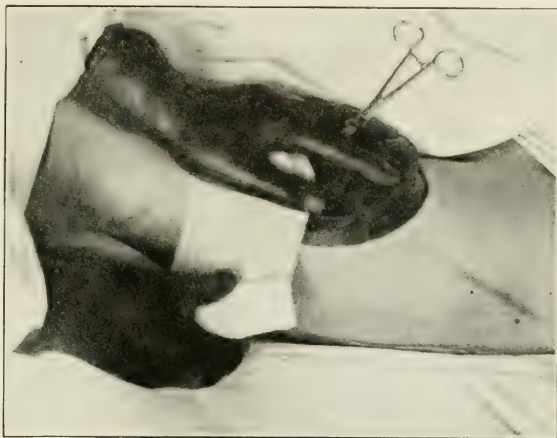


FIG. 49.—Appliance being bandaged to a wounded thigh. (Taylor.)

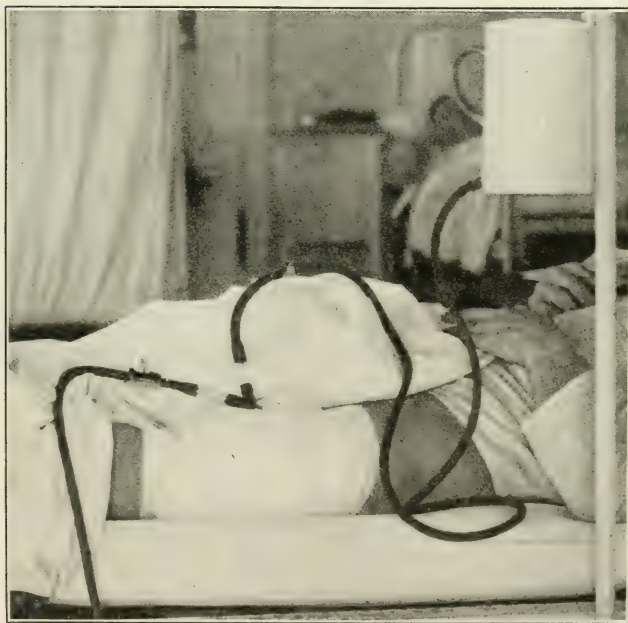


FIG. 50.—Apparatus applied, the inflow tube connected with an irrigating can held by a stand beside the bed and the outflow tube joined to a length of rubber tubing leading to a waste pail below. The appliance is completely covered by the bandage. The patient is able to conduct the irrigation himself. By opening the pinch cock on the inflow tube and closing the one on the outflow the wound is filled. By reversing the procedure the fluid is siphoned off and negative pressure maintained by the weight of the column of fluid which hangs in the outflow tube. (Taylor.)

fair trial in the hands of other surgeons. In the early days Taylor used Dakin's solution, but, because of its tendency to irritate the skin, it was gradually abandoned for hypertonic saline solution. Thorough evacuation of wound secretions; drainage; scrupulous cleansing of the wound cavity and its lining granulations; with the minimum amount of trauma; hyperemia; lymphorrhea; and heat, are surgical principles this method makes possible. Their claim that these objects can be attained by this tidal method, with less troublesome detail than any other method of wound treatment heretofore suggested, seems possible.

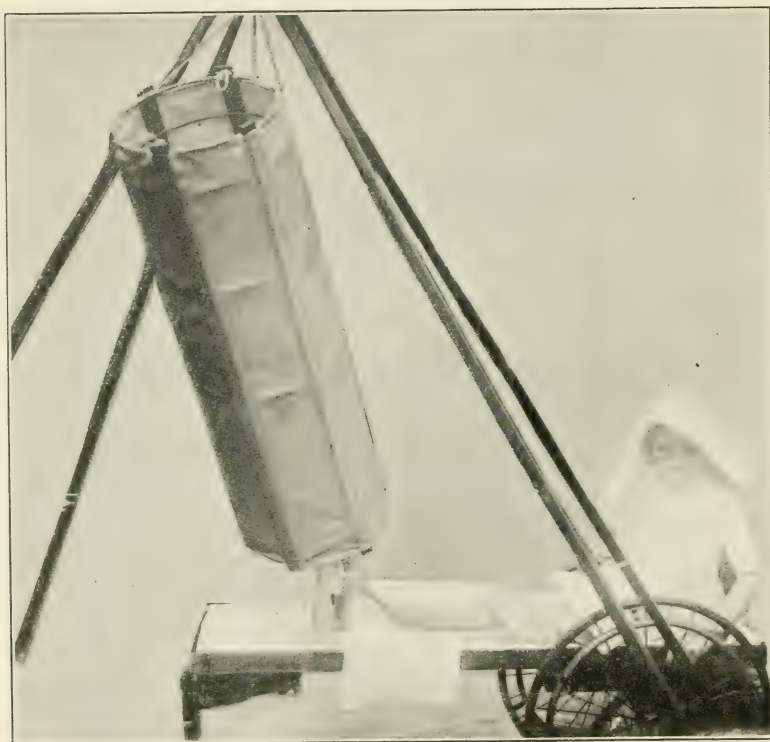


FIG. 51.—Method of applying lens treatment. (Lovett.)

**The Thezac-Porsmeur Method of Sun Treatment.** Lovett<sup>76</sup> described a series of carefully observed cases of chronic suppuration in the orthopedic service at the Children's Hospital by the so-called Thezac-Porsmeur method.

The principle of the treatment is the concentration of the sun's rays by means of a double convex lens. The lens has a diameter of 12 inches and a focal length of 72 inches. At the focal point, of course, the heat is great, as it would be in any lens used as a burning glass, therefore the patient should be placed beyond the focal point where the focussed sun's

<sup>76</sup> Journal of the American Medical Association, April 3, 1920, lxxiv, 944.

rays form a circle of from three to five inches in diameter. The degree of activity to which it is desirable to submit the wound can be regulated by carrying the lens nearer or farther away.

The lens is mounted in a canvas cylinder, one foot in diameter and three feet in length, which is kept rigid by two circular wires with thin strips of wood running from one loop to the other, over which the canvas is stretched. The lens is placed a few inches from one end of the cylinder. The advantage of this cylinder is that it enables the lens to be pointed directly at the patient and makes the application of the treatment more definite. The cylinder carrying the lens is mounted on a swivel and can be swung in any direction by means of a handle. The duration of the sun treatment should lengthen progressively. The first treatment should last for about five minutes a day and increase at the rate of about five minutes a day up to thirty minutes. The skin around the wound should be, as a rule, protected by towels, and the person giving the treatment should wear colored glasses, while the eyes of the patient are also protected if they are exposed to the glare of the circle of light.

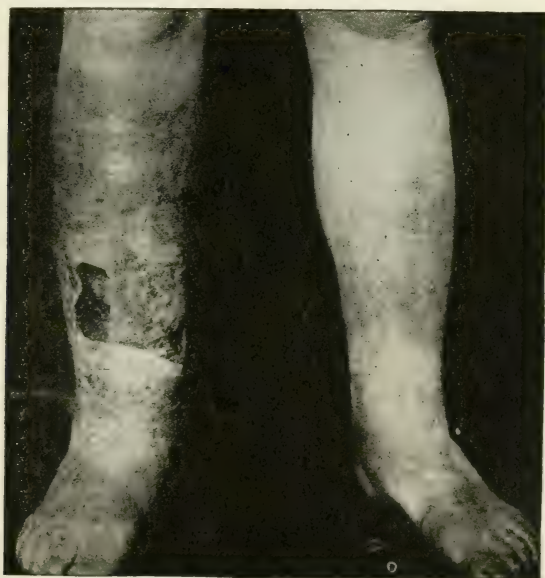


FIG. 52.—Case 2. Superficial ulcer of anterior crural region of right leg. The ulcer has been present at intervals for twenty years. Slight excoriation of the left leg has been present for one year with marked eczema and extensive varicose veins of both legs. (Morris.)

The effect of the treatment on suppurating wounds was definite.

1. The discharge immediately increased and then decreased.
2. Pale granulations took on a healthier color.
3. Sensitiveness diminished.

Lovett feels that the value of the treatment was demonstrated in cases of chronic suppuration from tuberculosis, syphilis and chronic osteomyelitis.



**The Deeper Structural Changes Arising from Varicose Ulcerations.** Morris<sup>77</sup> states that it is not generally recognized that changes in the structures remote from varicose ulcers quite regularly accompany the process when this is of long duration. These changes are so regular and striking that their significance deserves emphasis. It is not the tissues immediately beneath the ulcer in which these changes occur, in fact it is most unusual for periostitis or osteomyelitis to localize beneath an ulcer even of moderate depth. Instead, the tibia or fibula, and usually both, are involved in so diffuse a process as to extend throughout the entire shaft and involves even the epiphyses.

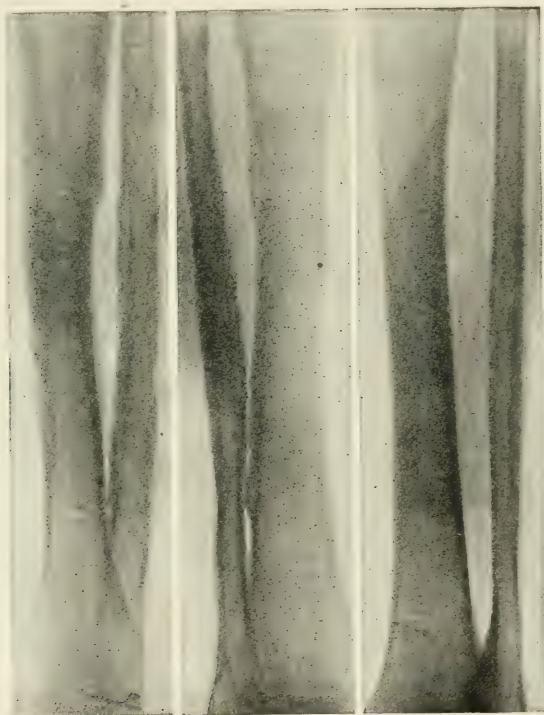


FIG. 53

FIG. 54

FIG. 53.—Case 2. Roentgenogram of the right leg, showing extensive periosteitis and osteomyelitis of both bones with narrowing and irregularity of narrow cavity. Calcification of vessels has been present but has not been marked. (Morris.)

FIG. 54.—Case 2. Roentgenogram of left leg, showing slight calcification of vessels. Little or no bone changes. (Morris.)

Inflammatory processes which result even in the most extreme structural changes never apparently reach the stage of abscess formation and, if suppuration exists, its products are absorbed into the system. Morris feels that the solution of this problem is probably furnished by the extensive vascular changes which quite regularly accompany these cases.

<sup>77</sup> Surgery, Gynecology and Obstetrics, January, 1920, No. 1, xxx, 72,



FIG. 1.—2d and 3d degree burn on a child's back, chest, abdomen, forearms, hands and face. 14th day after admission to hospital. (Lee.)



FIG. 4.—End-result after one year. Compare with Figs. 1, 2 and 3. (Lee.)



FIG. 2.—45th day—same patient. Surface of wound was sprayed with dichloramine-T in chlorococaine through the meshes of the gauze. No other dressing. Patient kept under a tent and temperature maintained with several large electric light bulbs. (Lee.)



The *chlorine group of antiseptics*, which were reviewed in detail last year, are finding a definite place in the treatment of infected wounds. Beyond almost uniformly favorable comments upon their clinical use, little has been contributed to this subject. That the unusual care and accurate technic demanded when the chlorine antiseptics are employed is warranted by the improved results obtained, we feel cannot be disputed. Nor is it justifiable, at the present time, in view of the possibilities offered by these methods, for surgeons to make excuses to avoid employing them.

**THE GERMICIDAL VALUE OF POTASSIUM MERCURIC IODIDE.** Since 1914, MacFarland<sup>80</sup> has been working with this substance and he feels that it has four distinct and valuable features making for its superiority over other salts of mercury and iodine.

It is readily soluble in both water and alcohol as well as in acetone.

**PICRIC ACID FOR THE PRE-OPERATIVE DISINFECTION OF THE SKIN.** Gassegrain,<sup>81</sup> following Dr. Gibson's suggestion, tried this method and reports very favorably upon the result. He advocates the use of picric acid as a pre-operative skin disinfectant, because:

1. It thoroughly disinfects and can be used with soap and water.
2. It does not irritate the skin.
3. It is approximately 40 per cent. cheaper than the drug now almost universally used for the same purpose.

Churchman<sup>82</sup> in his experimental work with GENTIAN VIOLET refers to its action upon bacteria as "bacteriostatic." He feels that this describes with nice accuracy the action of the dye, which is merely to delay growth, and that the apparent death of the organism, following exposure of the dye, is not real. This conforms with the clinical experience of surgeons working with the overseas forces when employing such dyes as flavine, brilliant-green, etc. In the clinical work at the Walter Reed Hospital, two types of wound were treated with gentian violet. Amputation stumps that had become diphtheria carriers, and amputation stumps with ordinary infection. One of the most difficult problems at the hospital had been the infection of a number of thigh amputations with wound diphtheria and these patients had become diphtheria carriers. The fact that *Bacillus diphtheriæ* is gram-positive and will not grow in mediums containing minute amounts of gentian violet were sufficient reasons for assuming that it might kill these organisms in the wounds. Both the cases were free of the organisms in a very short time.

He also tried the use of the gentian violet in unhealed stumps containing other organisms. Unfortunately, he only reports 4 cases from which we think it is hardly fair to draw any conclusions. With such a quantity of clinical material as was presented at the Walter Reed Hospital, the natural query is the limiting of his experiment to 4 cases.

**Peripheral Nerve Surgery.** In considering the regeneration of peripheral nerves, after division, Lewis<sup>83</sup> states that definite evidences of

<sup>80</sup> American Journal of the Medical Sciences, April, 1920, No. 4, cxlix, 586.

<sup>81</sup> New Orleans Surgical Journal, January, 1920, No. 7, lxxii, 398.

<sup>82</sup> Journal of the American Medical Association, January 17, 1920, No. 3, lxxiv, 146.

<sup>83</sup> Ibid., July 10, 1920, No. 2, lxxv, 73.



regeneration are noted within a few hours in the proximal segment adjacent to the point of injury. Though some of these early changes are undoubtedly abortive, others indicate attempts at repair. Some degenerative changes occur in the neuraxes in the distal end of the proximal segment, they do not, however, extend far back in the nerve, probably only to the next node of Ranvier.

Definite regeneration of neuraxes occurs only in the proximal segment of the nerve, and all the neuraxes, that eventually neurotize the distal segment of the nerve passing into the motor end-plates and sensory endings, develop from these neuraxes which regenerate from the proximal segment. By the eighth day after division of the nerve, the medulated fibers of the proximal segment have given off numerous lateral rami, some as high as 5 mm. above the point of section, and these fibers grow distally beneath the old neurilemal sheath. The non-medulated fibers also divide into bundles of neurofibrillæ which grow down in the old sheaths by the fourteenth day. In studying the repair of nerves through a gap, it can be positively demonstrated that no neurofibrillæ can be found in the distal segment until those developing from the proximal segment have bridged the gap. There are no evidences at the present time that peripheral regeneration of a divided nerve ever occurs.

The changes that occur in the distal segment after division are just as important as those occurring in the proximal. For the transmission of the nerve impulse there must be intact neuraxes, and these neuraxes cannot reach their terminal distribution in the end-plates unless they are guided by bands or conduits through which they can creep. The distal segment of the nerve through which these neuraxes must pass undergoes both degenerative and regenerative changes following a division. The neuraxes degenerate, while the myelin sheaths early show evidences of growth and repair. In this repair of the sheaths in the distal segment, by the fourth to sixth day, definite protoplasmic bands are formed; appearing earliest in the part of the segment nearest to the line of division and last in the part furthest away. These bands evidently play an important role in nerve regeneration; for the fibers which have no neurilemmal sheaths, such as those of the optic nerve and spinal cord, do not regenerate after division.

Stewart and Cadwallader<sup>84</sup> report in this connection the end-result, after eighteen years, of a case of severed spinal cord following a gunshot wound, in which myelorrhaphy was performed within three hours after the injury. No return of function had occurred. It is perhaps the best clinical evidence on record that even under the most favorable conditions for surgical procedure regeneration of the spinal cord does not take place after complete section and end-to-end suture. Kirk and Lewis were able to demonstrate these protoplasmic bands passing through and bridging the gap between the divided ends of a nerve in which fascial tubulization had been performed. They seemed to precede the developing neuraxes, forming pathways, as it were, for these as they developed.

<sup>84</sup> *Annals of Surgery*, June, 1920, No. 6, lxxi, 719.

In other words, the Wallerian degeneration of the neurilemmal sheaths in the distal segment are followed by the formation of these protoplasmic bands which form new sheaths or tubules through which the developing neuraxes creep toward their terminal connections.

All surgical aids to the repair of divided nerves must, of course, be based upon a knowledge of these histological changes. After the division of a nerve the cut fibers retract within the epineural sheath, and a connective-tissue cap forms over the ends of the nerve composed of cells of the endoneurium and perineurium and surrounding tissues. This so-called neuroma will develop within nineteen days. The neuraxes growing from the proximal end are turned back on themselves and in many instances as they reach the connective tissues form the spirals described by Perromcito. The neuromas are composed of connective tissue and neuraxes which have been thwarted by the scar tissue in their attempts to enter the distal nerve segment. Though some of the growing neuraxes may succeed in passing around such scar tissue and reach the distal segment, it is doubtful whether they will reach the terminal connections to which they were originally destined. Thus scar tissue, which forms after division of the nerve, seriously interferes with nerve repair. There will be few successes in repairing such injuries unless all of this scar tissue is resected. He believes it advisable in many cases to employ frozen sections to determine the level to which the resection of the neuroma should be carried. The time occupied by the mobilization of the ends of the nerve and the preparation of them for accurate adjustment could easily be utilized for the making of such frozen sections.

He emphasizes that success in peripheral nerve repairing depends on accurate anatomic approximation of the divided ends. Stoffel has described a definite topography of peripheral nerves and insists that the sensory and motor funiculi, which serve different muscles, maintain their position and relation throughout the entire course of the nerve which makes necessary a non-axial rotation of nerve trunks during their suture, thus avoiding distortion of the nerve pattern. If the nerve pattern is destroyed, reëducation of the muscles or readjustment becomes necessary, for the developing neuraxes may not reach the muscles for which they were originally intended or may even be diverted to the skin.

He feels that to perform funicular suture is the object to be desired, but his attempts have met with little success. As perfect anatomic repair as is possible should be secured, and the surgeon who makes the most perfect anatomic repair will, other things being equal, have the greatest number of successes. Imperfect redistribution occurs to some extent after every suture, and this can be overcome more or less successfully by reëducation or by the subsequent degeneration of the fibers which have made wrong terminal connections.

**THE IMPORTANCE OF EARLY SUTURE.** If the resection of all scar tissue is the first important factor in determining the success of nerve suture, preservation of the internal topography of the nerve is the second factor, and the length of time intervening between the division of the nerve and its repair is the third important factor. Those cases in which



nerve suture is performed early, within three or three and a half months, have a higher percentage of recovery than those in which the suture is delayed beyond this period. The importance of the time element cannot be emphasized too strongly, for there is a tendency in civil practice to delay operation with the hopes that improvement may follow the use of massage and electricity, if they are continued long and faithfully. He also calls attention, as did Andrew Woods several years ago, to the misleading supplementary movements assumed by uninvolved muscles and which are not the result of regeneration of the injured nerve. These movements are often mistaken as evidences of recovery and because of this operation deferred.

**END-TO-END SUTURE.** End-to-end suture is the only procedure that can be relied on to reestablish the continuity and function of a nerve after division. He advises epineural sutures of fine silk or catgut, and where traction must be exerted, one or more transfixion sutures may be employed. The epineural sutures should be so applied that the sheath is entirely closed to prevent the straying of the neurofibrillæ into the surrounding tissues. As one's experience in peripheral nerve surgery increases, the attempts at end-to-end suture are more and more successful, even in long defects. By dissection of a nerve from its bed mobilization of the segments will usually be sufficient to obtain approximation.

**CABLE TRANSPLANTS.** Experimentally, auto and homo cable transplants will conduct neuraxes from the proximal to the distal segments. Fascial tubes can also be used with success experimentally. Clinically, however, the results of these procedures are not encouraging.

In eighteen operations analyzed by Platt,<sup>85</sup> in which fascial tubulization, combined with autogenous nerve graft, were used, there was complete absence of any sign of recovery in all of them. Secondary exploration in 4 cases shows complete silence of the nerve trunk to direct electrical stimulation. At the reexploration operations, partial or complete obliteration of the lumen of the fascial tube was noted. He is of the opinion that the early reexploration of all grafts and fascial bridge operations is advisable.

Lewis employed auto cable transplants in 12 cases and tubulization with fascia in 6 cases, and in none of them has there been a recovery.

*Procedure for Physiologic Interruption.* There is a group of nerve injuries in which there is no anatomic division but a physiologic interruption of nerve impulses by constricting bands, thickened epineurium, bony callous and cicatricial nodules within the nerve resulting from intraneural hemorrhage and proliferation of intraneural connective tissues. Neurolysis is of value in those cases in which paralysis has existed for months and in which a distinct return of motive power may occur within ten days following the operation. Whether neurolysis or resection is to be performed depends upon the patient's feeling in the nerve and the electrical reaction. The time element here is an important factor in determining the results after neurolysis. The greatest number

<sup>85</sup> British Journal of Surgery, London, January, 1920, No. 27, vii, 384.



of improvements, 80 to 100 per cent., are found in cases in which this operation was performed within five months after the injury. A number of methods have been suggested to prevent the reformation of scar tissue after neurolysis. It is usually possible in the majority of cases to place the liberated nerve between uninjured muscles. They should not be placed in contact with cut muscle fibers, for the adhesions which then form may seriously interfere with the conduction of the nerve impulse. Fascia cannot be used for this purpose for it becomes converted into scar tissue, and in 3 cases that he has re-operated, where a fat transplant had been used, the fat had all been replaced by adhesions.

**RECOVERY OF FUNCTION.** The order of recovery of function of nerves is fairly constant. The musculocutaneous nerve in the arm recovers the most rapidly and completely. The musculospiral next. The internal popliteal, then the median and most slowly the external popliteal. Changes in muscles and joints develop during the repair of the nerve unless prevented or corrected, and will often defeat the purpose of the operation. There should be the closest coöperation between the physiotherapist and the surgeon. Stookey's article was referred to in last year's *PROGRESSIVE MEDICINE*, December, 1919, page 262, and is very complete.

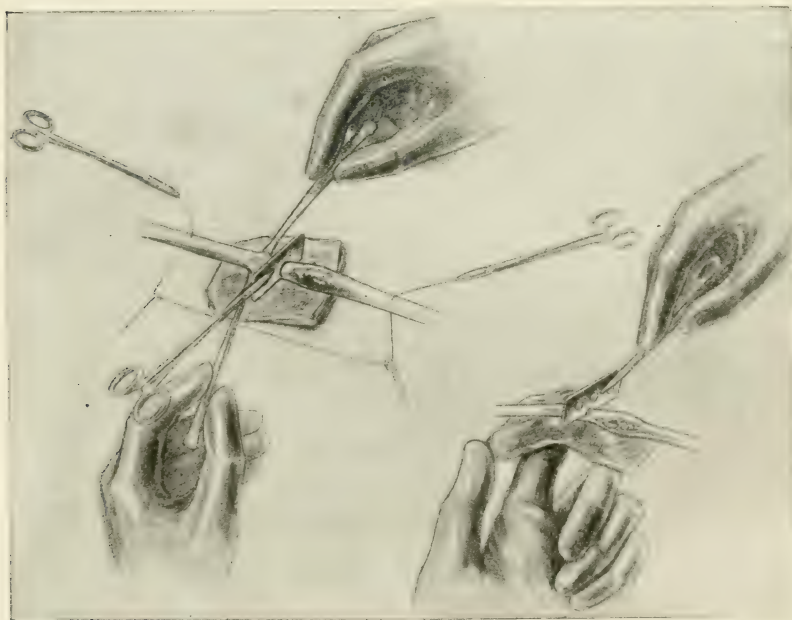


FIG. 55.—Shows method of sectioning nerve with safety razor.  
(Frazier and Silbert.)

Frazier and Silbert,<sup>86</sup> summarize the principle of peripheral nerve surgery as follows:

<sup>86</sup> *Surgery, Gynecology and Obstetrics*, Chicago, January, 1920, No. 1, vol. xxx.

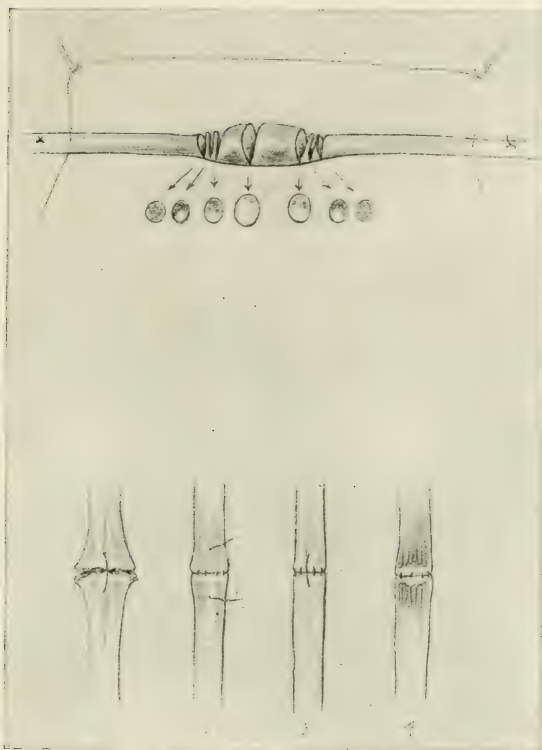


FIG. 56.—Steps in technic of nerve suture. (Frazier and Silbert.)

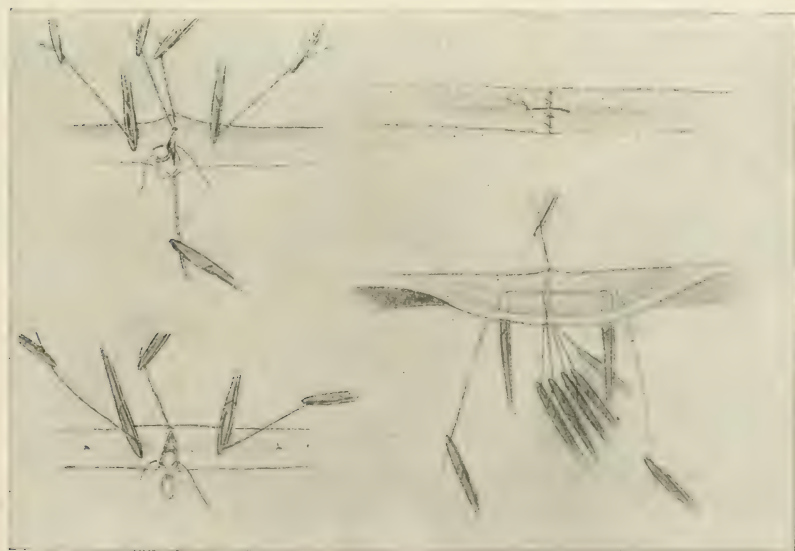


FIG. 57.—Steps in technic of nerve suture. (Frazier and Silbert.)

Liberation or neurolysis is to be preferred in the absence of complete anatomic division or a neuroma in continuity. Usually, after excising all the scarred tissue and laying bare the nerve sheath, there is a quick response to faradism. In the presence of a neuroma or anatomic division of the nerves, resection and suture are only to be considered. Resection should be carried upon both the proximal and distal ends until healthy scar-free fasciculi are exposed. In bridging defects, the transplantation of nerve should be the last resort. Nerve stretching, mobilization, transposition, as of ulnar and muscle spiral nerves, are to be chosen instead of transplantation. When these fail, a nerve transplant is justifiable. The autotransplant being first choice and the homotransplant (preserved in liquid petroleum, or 50 per cent. alcohol) the second choice. For autotransplant, the musculocutaneous or crural nerves of the leg, the radial or internal cutaneous nerve of the arm may be selected. Sharp, clean dissection, careful hemostasis, the approximation of healthy tissue, without undue tension, represent the tripod upon which successful nerve suture rests.

THE TECHNIC OF NERVE SUTURE AND NERVE GRAFTING. Elsberg<sup>87</sup> emphasizes, as every one else does, that from the beginning to the end of the operation, surgery of the peripheral nerves requires a perfect technic. One minute fault in technic—whether it be the failure to obtain a dry wound, too rough handling of the nerve trunk, insufficient excision of scar tissue, from the bulb or from around the nerve, improper application of the sutures, all diminish the chances for nerve regeneration.

He outlines *five principles in suture of peripheral nerves*:

1. *Identification of the Injured Nerves.* This requires care, patience and a good knowledge of anatomy. If a normal part of the nerve, or nerves, below and above the incisions, is first exposed and the surgeon then works from normal to scar tissue, the identification of the injured nerves is always possible.

2. *Exposure.* The lower ends of the nerves should be first exposed and freed, because it is the degenerated end. The upper end should be exposed for as short a distance as possible, and should be very carefully handled.

3. *Examination for Nerve Bundles.* He advocates the examination for, and isolation of, uninjured nerve bundles and advocates their being saved. In a considerable number of patients some perfectly good nerve bundles are preserved on the surface or in the deep parts of the bulb, and such nerve bundles may be freed from the scar tissue and not divided. When they run through the center of the bulb, their isolation is much more difficult and will hardly warrant the time required to attempt their preservation. This procedure is not advocated by other surgeons.

4. *Excision of the Bulbous Enlargement or of the End-bulbs.* When there is complete anatomic separation of the nerve, the bulb should be divided transversely, with a safety razor blade preferably in successive sections until normal fasciculi are readily recognized. Usually there is

<sup>87</sup> Journal of the American Medical Association, November 8, 1919, No. 19, lxxii, 1422.



fairly active bleeding from the intraneuronal bloodvessel when normal funiculi are reached, this is especially true in the sciatic and median nerves. This bleeding rarely requires ligature and is usually controlled with warm saline solutions.

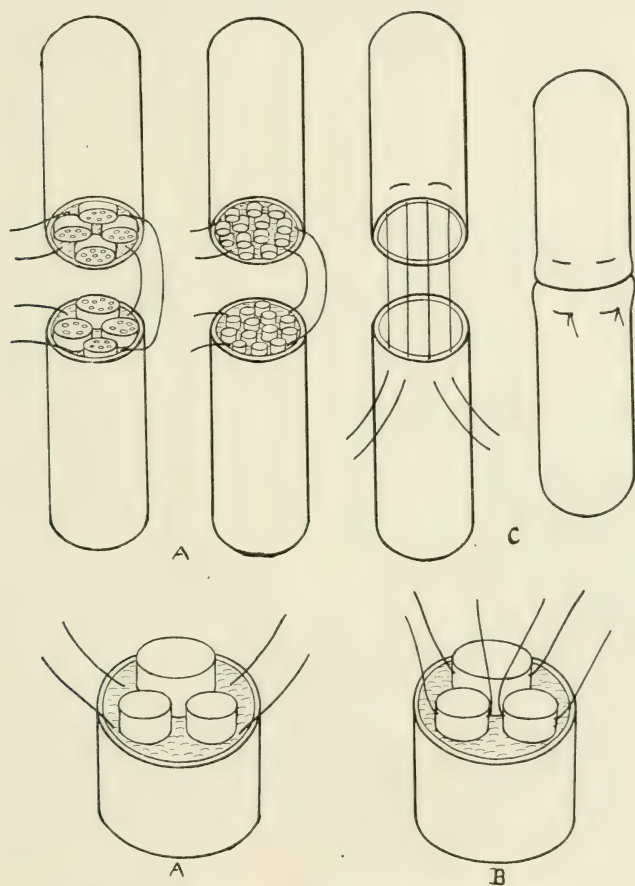


FIG. 58.—A, dissection in which the perineural sutures are passed; B, transfunicular suture, which should never be used; C, epineurial mattress sutures. (Diagrammatic.) (Elsberg.)

5. *The Prevention of Rotation of the Nerve Ends and Distortion of the Nerve Pattern.* The ideal apposition of the ends of the nerve would be one in which the cut ends of each funiculus is placed exactly opposite to its corresponding end, but in practice this is impossible. He believes that ideal peripheral nerve surgery will only be possible when we have learned a great deal more of the minute structure of the peripheral nerves, and the arrangement of fibers and bundles of fibers to form the nerve patterns.

6. *Approximation of the Divided Ends of the Nerve.* The approximation should always be made without tension. When mobilization of the ends does not provide sufficient length, further relaxation can be obtained by flexing the joints (flexion at the wrist for injury of the ulnar and median nerve in the forearm; flexion at the elbow for median and musculo spiral nerves in the arm and forearm; extension at the elbow and adduction of the arm for the ulnar nerve in the arm and forearm, flexion of the knee, plantar of the ankle for nerves of the lower extremity). Transplantation of the ulnar nerve to the front of the internal epicondyle is often necessary when dealing with the ulnar nerve in injuries above or below the joint.

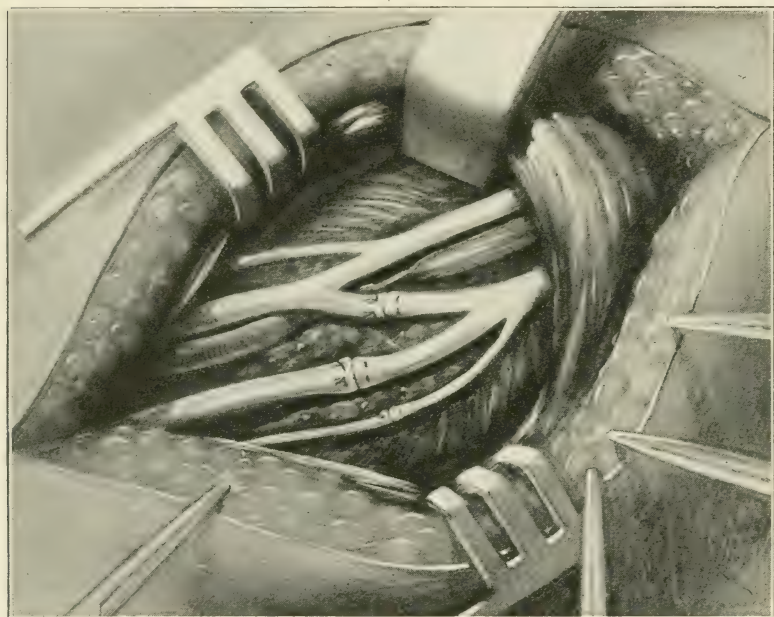


FIG. 59.—Suture of the outer head of the median nerve and the ulnar and the internal cutaneous nerves, showing epineural mattress sutures. (Elsberg.)

**Treatment of Causalgia.** Lewis and Gatewood<sup>88</sup> say that Weir Mitchell during the Civil War gave the name causalgia to the burning and throbbing pain, which have been compared to the sensation produced by pin pricks, so frequently complicating or becoming a sequelæ of peripheral nerve lesions. This pain never ceases, even at night, and may be aggravated by any number of causes and finally becomes paroxysmal.

No idea of its frequency can be determined from statistics because of the wide variation in the interpretation of this condition. Only

<sup>88</sup> Journal of the American Medical Association, January 3, 1920, No. 1, vol. vii.

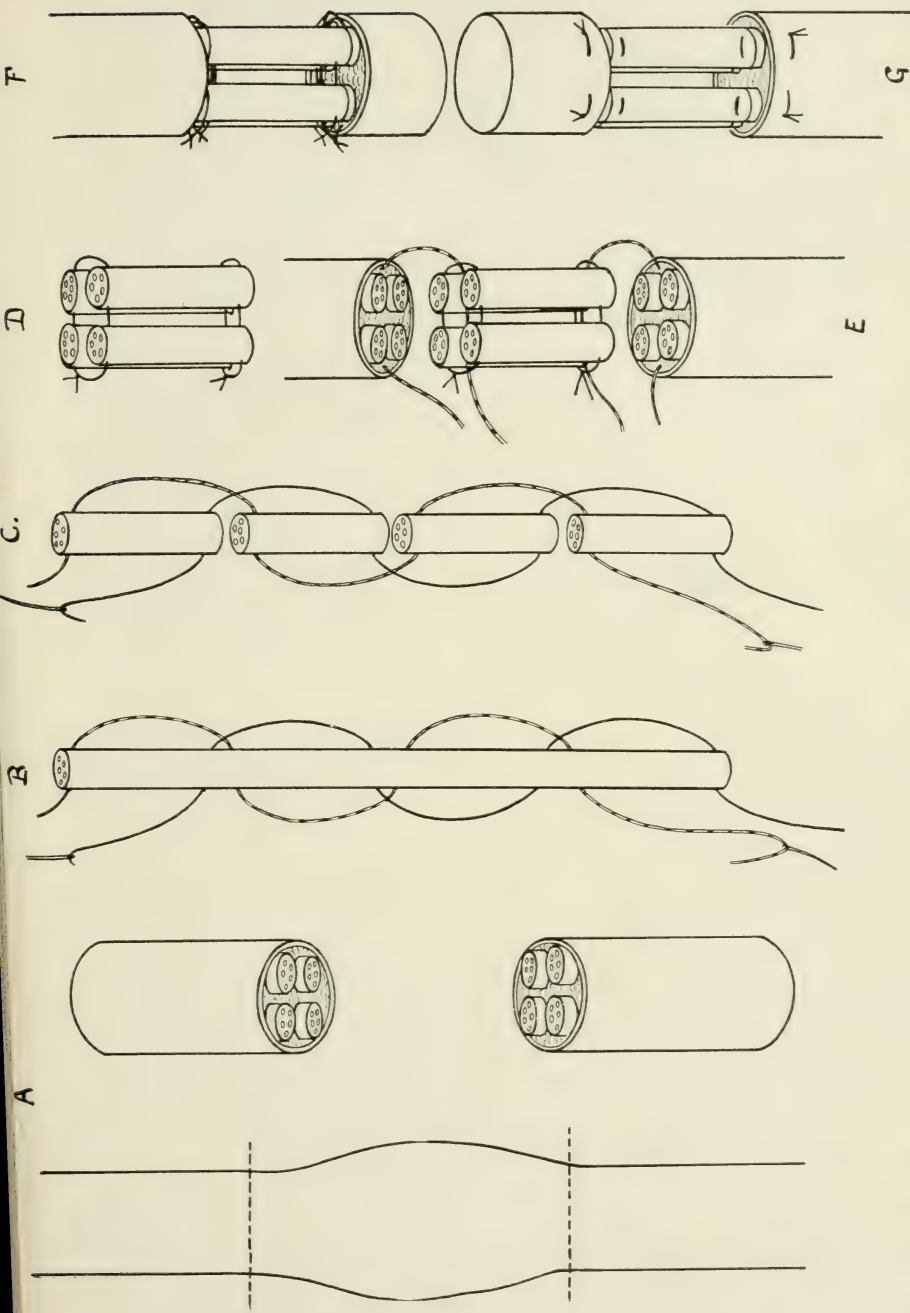


FIG. 60.—The cable graft: A, bulb, resected and ends of the nerves exposed; B, sutures passed through the cutaneous nerve used from cable graft; C, nerve divided into segments; D, cable graft ready for transplantation; E, sutures passed through ends of cable graft and ends of nerve; F, sutures tied; G, perineural sutures tied. (Diagrammatic.) (Elsberg.)



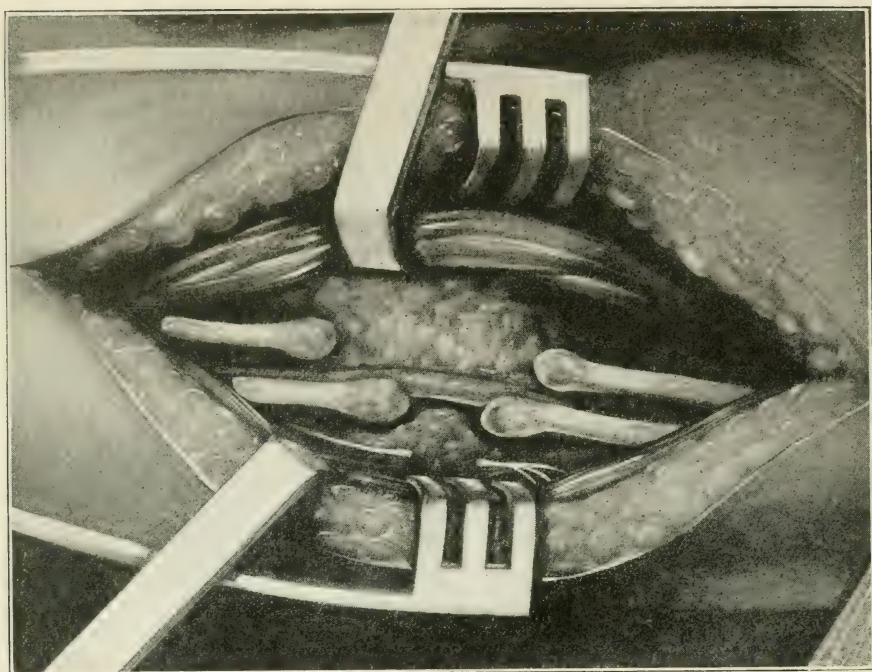


FIG. 61.—Median and ulnar end-bulbs. (Elsberg.)

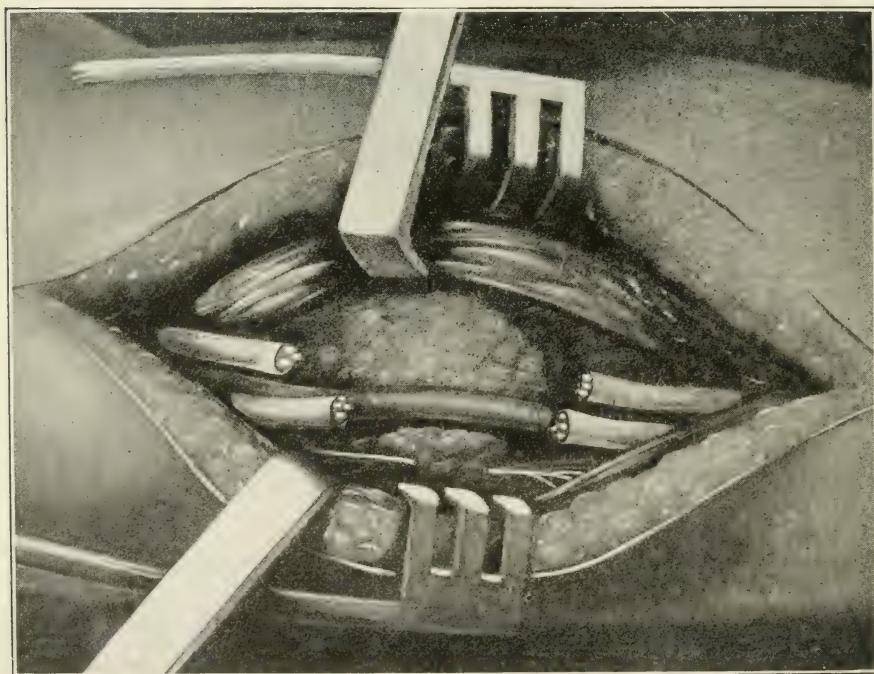


FIG. 62.—Bulbs resected. The defect has to be filled in by a graft. (Elsberg.)

intense paroxysmal pain should be regarded as causalgia. Four cases of causalgia were noted among the 550 cases of peripheral nerve injuries observed at U. S. General Hospital No. 28.

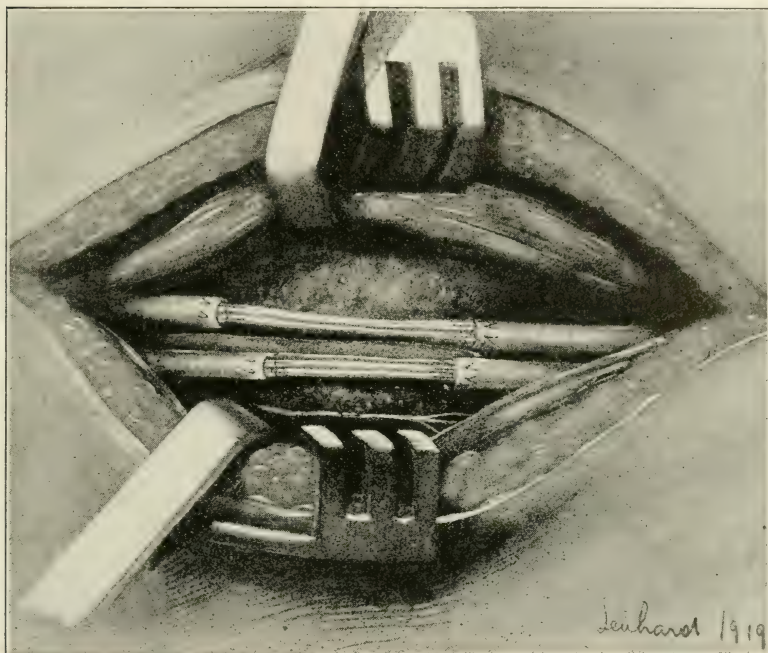


FIG. 63.—Cable grafts in place, bridging over defects in median and ulnar nerves; epineural stitches have been tied. (Elsberg.)

Weir Mitchell believed that the pain was due to an ascending neuritis which might be a complication in any injured nerve and that the process gradually involved all the nerves of the extremity affected. As a result of surgical experience, it has been found that the median nerve is involved most frequently in causalgia affecting the upper extremity, and the internal popliteal in causalgia involving the lower extremity. When an ulnar lesion is accompanied by intense pain, it is usually due to an associated lesion of the median nerve, or to an injury of the brachial plexus affecting both ulnar and median nerves. Lewis, in describing the pathology, includes such lesions as a swelling and edema of the nerve trunk, small neuroma, and even foreign bodies in the neighborhood of the nerve. Several of the cases he reported were surrounded or imbedded in scar tissue. Leriche would eliminate cases where there are definite mechanical or pathological lesions in the nerve or adjacent tissues, and confine the term to those cases in which no definite cause can be discovered. He applies the term to the group in which no such etiological causes can be found, and feels that it is a vasomotor phenomenon, and



advocates a division of the sympathetic nerves in the arterial sheath by an incision encircling the sheath of the artery, which he calls periarterial sympathectomy. Lewis advocates the injection of 60 per cent. alcohol into the nerve trunk after all other obvious pathological conditions have been surgically removed, as scar, foreign bodies, neuromata. When this injection is made, the nerves to be injected should be exposed while the patient is under a general anesthetic. After completing the surgical part of the procedure, the injection should be made above the site of the injury, for when made below the results have only been temporary.

**Arteriovenous Aneurysms Treated by Intrascapular Method of Suture.** Matas<sup>89</sup> says that renewed interest in the treatment of arteriovenous aneurysms has been roused by the great frequency of these lesions during, and following, the late war. The coincident injury of the artery and its companion vein has long been recognized as one of the most frequent and characteristic injuries of bloodvessels in modern warfare. The frequency in the late war, however, has exceeded that of all previous records. With the advent of the hard jacketed, high velocity projectile and small caliber rifle, the history of war aneurysms begins. The explanation is that modern warfare is carried on by preponderance of artillery and machine gun fire. This varied during the war. In the early part, 1914, to the latter part of 1916, the machine gun missiles predominated. Chalker and Glenard report that a little over 50 per cent. of their wounds were caused by rifle bullets. Lee<sup>90</sup> reported that at the American Ambulance, during the same period, the rifle ball wounds were close to 80 per cent. Subsequently, and during 1918, the artillery wounds were in preponderance, almost in a reversed relation. Bier and Küttner make the same observation on the German side. The frequency of vascular injuries is indicated by the report of Hay and Bowlby that during the first battle of the Somme they treated 277 wounds of individual vessels.

Okinczyk,<sup>91</sup> in a French Ambulance, reports 24 per cent. of the wounded requiring special attention for injuries of the bloodvessels. In the military hospitals at the base, the effect of the first aid treatment at the front and the lines of communication were found to have lowered the proportion of gunshot wounds of bloodvessels to about 2 per cent. [This is a misleading statement if taken at its face value for it fails to record the percentages of deaths from vascular wounds which occurred before the patients reached the base hospitals and this was not a negligible quantity, Reviewer.]

Sir George Makins,<sup>92</sup> in an analysis of 272 war aneurysms admitted to the London Hospital, found that 120 were arterial and 150 arteriovenous; and that of the latter, a little over half, were simple or direct

<sup>89</sup> *Annals of Surgery*, April, 1920, No. 4, lxxi, 403.

<sup>90</sup> *Proceedings of Philadelphia College of Physicians*, 1916.

<sup>91</sup> *Jour. de Chirurgie*, 1917, xiv, 441.

<sup>92</sup> *Gunshot Injuries of the Bloodvessels*, London and New York, 1919.



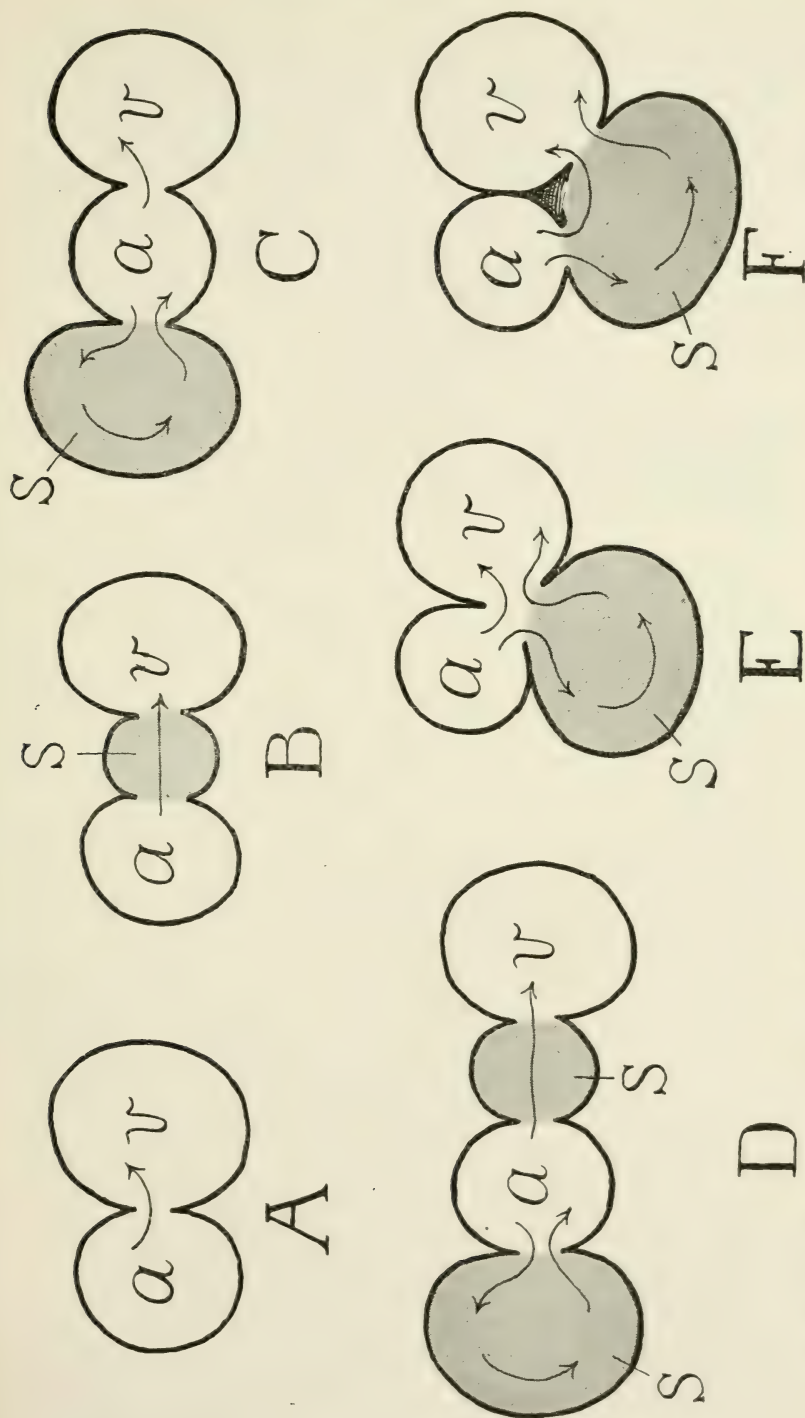


FIG. 64.—A, simple aneurysmal varix. B, arteriovenous aneurysm (so-called varicose aneurysm) sac interposed. C, arterial aneurysm combined with aneurysmal varix. D, arterial and arteriovenous sac. E, arteriovenous sac with common opening of communication with artery and vein. F, arteriovenous sac with separate openings of communication with artery and vein. (Modified from Makins.) (Matas.)

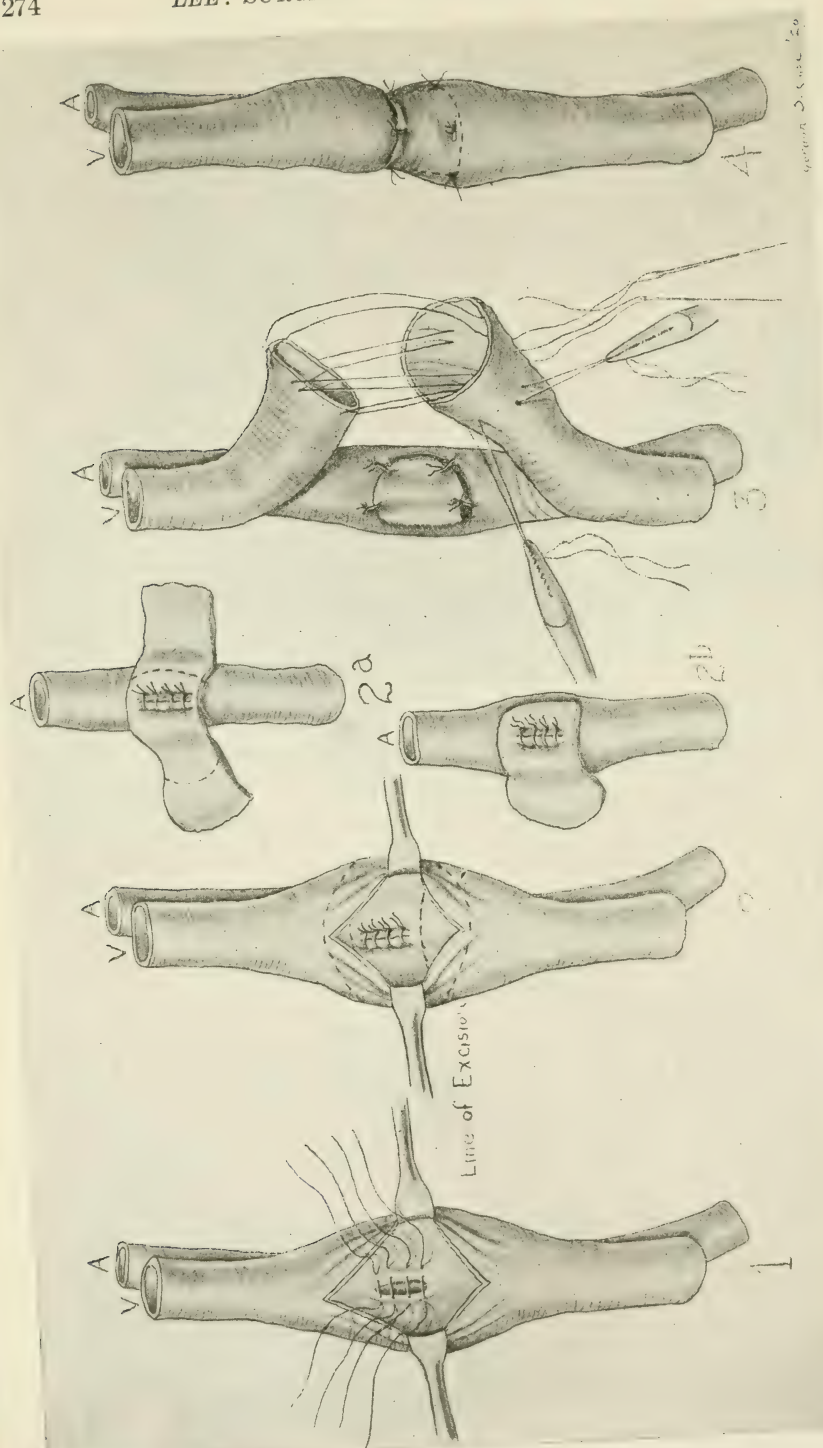


FIG. 65.—One of the methods of closing an arteriovenous fistula (aneurysmal varix) by the transvenous route (Matas-Bickham procedure), modified by Dr. J. Chalmers Da Costa (Philadelphia, Pa.). (Matas.)

aneurysmal varices. He, in accordance with the majority of observers, finds that these bivascular or arteriovenous injuries occur with the

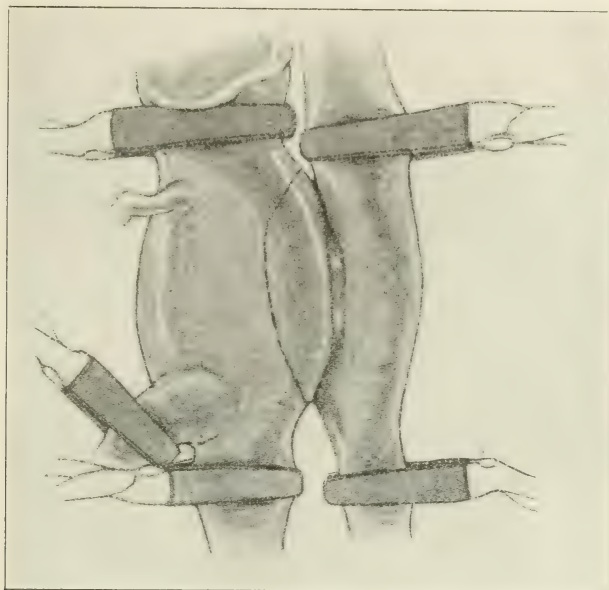


FIG. 66.—Detail of anastomosis to show line of incision on the vein in order to expose the interior of the sac. (Matas.)

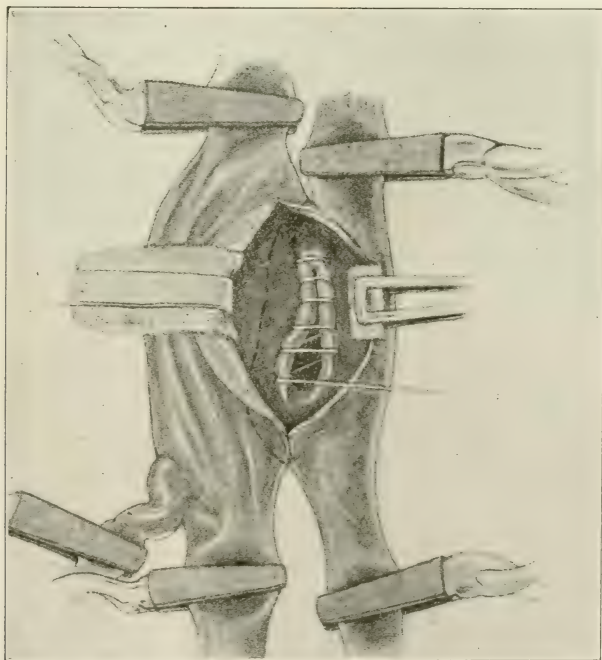


FIG. 67.—Interior of the sac, showing closure of the orifice of communication by continued silk sutures. (Matas.)



greatest frequency (from the records in the base hospitals) in the carotid, femoral, popliteal and axillary tracts—though at the front, the tibial vessels were more frequently injured, 26.6 per cent., but as they are usually a complication of fractures, they are treated and recorded simply as fractures.

In a general way it may be stated that of the traumatic war aneurysms, fully 50 per cent. involved both the artery and the satellite vein, and, furthermore, that in fully 50 per cent. of the arteriovenous aneurysms the communications established between the vessel is of the simple direct fistulous type (aneurysmal varix), and in the remainder the wounded

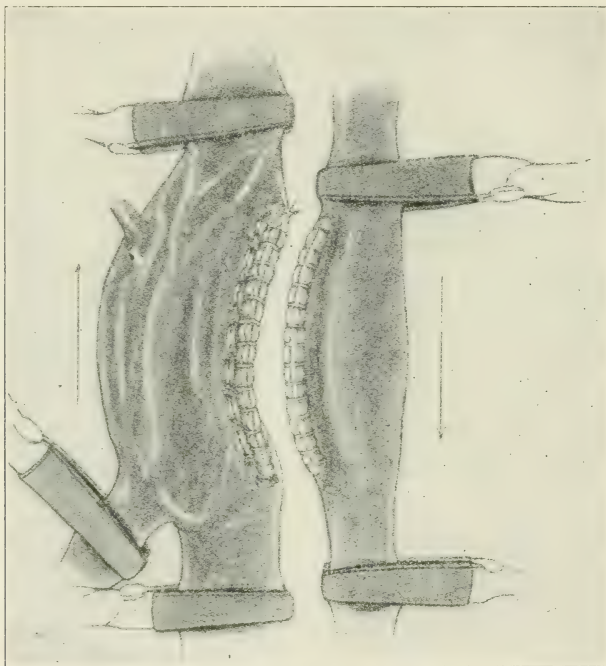


FIG. 68.—The anastomosis closed; artery and vein detached, isolated and separately closed by lateral arterio- and phleborrhaphy. The arterial orifice has been closed separately by intrasaccular suture on the venous side and the first line of intrasaccular sutures is reinforced at the expense of the vein. (Matas.)

vessels communicate indirectly through a pseudo or adventitious sack. Statistics show that by far the greatest number of these vascular lesions are caused by the small pointed rifle or machine gun bullet. In reviewing the general German literature of the war, Solomon found that 74 per cent. of the traumatic aneurysms were caused by rifle bullets. From all that can be gathered, the largest number of aneurysms were caused by the small rifle bullet as it sped through the tissues with high velocity, leaving only a clean cut, tunnelled perforation. On the other hand, the fragments of the shells or explosive projectiles of low velocity when retained in the tissues have caused vascular lesions in about 57 per cent. of the cases.

From his personal experience, Matas feels there is no single method or technic that is applicable to all varieties of arteriovenous aneurysms. Insurmountable and forbidding anatomical and pathological conditions will always be present in certain cases which will demand the radical

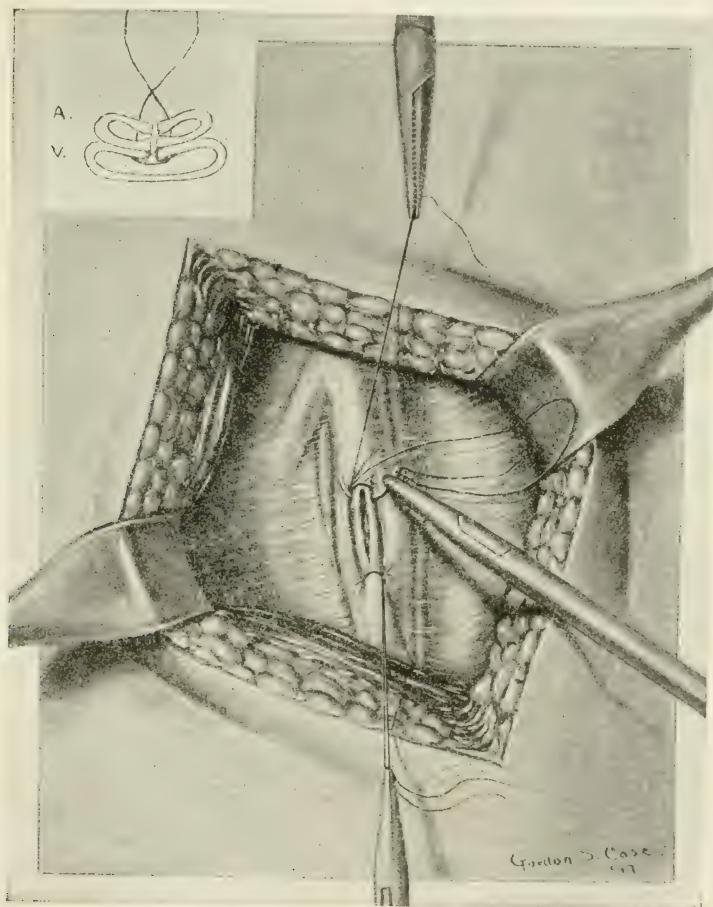


FIG. 69.—Case of Julius B. Arteriovenous aneurysm of the femoral vessels at the apex of Scarpa's triangle. Shows interior of large space occupied by hematoma, covered over with a veil of semitranslucent exudate in process of organization. First stage of suture. In the upper diagram (A) the needle is shown penetrating through both walls of the arteriovenous septum, so as to close the narrow fistula which connected both vessels. By lifting the walls of the collapsed and thin vessels with two traction sutures, one at each end, the curved needle was able to penetrate the septum and obliterate the orifice in the vein as shown in the sketch (B) without obliterating its lumen. (Matas.)

methods of ligation and extirpation, which in a measure are conservative if they accomplish their purpose of saving a limb or life. But, in Matas's experience, he feels that the application of many of his details of technic will materially reduce the number of radical ligations and extirpations which are undoubtedly performed in the current practice of the day.

In last year's review we called attention to the article by Goodman<sup>93</sup> upon the primary conservation of vascular injuries by suture, end-to-end anastomosis and intubation with paraffined glass tubes, and Matas commends these efforts at conservation.

It is possible, from a morphologic and pathological standpoint, to differentiate about fifteen varieties of arteriovenous aneurysms. However, they can be grouped into two fundamental types: The *aneurysmal varix* and the *varicose aneurysm*. The aneurysmal varix typifies the direct mode of arteriovenous anastomosis; the varicose aneurysm the indirect method of communication between the two vessels through a common, intermediary or communicating sac. In the aneurysmal varix the arterial and venous wounds become agglutinated and adherent, and an arteriovenous fistula is established. In the varicose aneurysm, the normal anatomical position of the vessels is disturbed, and, instead of lying side by side as in aneurysmal varices, their relations are distorted and they are joined as well as separated by a clearly differentiated and well-walled sac which is lined with endothelium continuous with that of the openings in the bloodvessels. The illustrations give a clear idea of the relations of the bloodvessels to each other and to the adventitious sac.

Suture of arteriovenous aneurysms by *endo-aneurysmorrhaphy* was performed by him in 12 cases. All made good recoveries except one of a carotid aneurysm which died on the eighth day.

*Lateral angiorrhaphy* in arteriovenous hematoma. He reports one case he performed in 1907 and quotes five others.

*The obliterative suture* in arteriovenous aneurysms of the varicose type is shown in illustrations 2, 3, 4, 5 and it shows the simplicity and safety of the technic of the intrasaccular suture in its obliterative aspects.

*The Treatment of Aneurysmal Varix or Fistula.* In this type, Matas applies a principle of endo-aneurysmal suture in its restorative phases which he feels has been followed by success that could not have been obtained by any other method.

1. Endo-aneurysmal suture by the transvenous route (Fig. 65) shows a modification by Da Costa of the original method devised by Bickham. Matas calls attention to the necessity of avoiding injury to the endothelium of the vein while exploring its interior preliminary to the transvenous suture. Irrigating with warm sterile salt solution instead of wiping the interior with gauze to clear the fistulous tract and then spraying with liquid vaseline. In introducing the suture to close the arteriovenous communication, he first passes the needle through a small portion of the fibrous tissues which binds the vessels together at the end of the communication. This is placed on the external aspect of the vessels entirely outside of them and between the two. This stitch, in addition, should not penetrate the intima of either vessel—thus resembling the commencement of the outer row of sutures in gastro-enterostomy. This stitch is immediately tied and then the needle is passed obliquely from without inward, emerging on the inner side of the vein

<sup>93</sup> PROGRESSIVE MEDICINE, December, 1919, p. 268.



close up to the extremity of the stoma. The extreme edges of the stoma are then brought together by fine continuous sutures passing through the intima and media until the opposite end is reached, when the needle is again passed out from the lumen of the vein obliquely through its wall and the overlying tissues which bind it to the artery, so as to emerge between the two vessels, when it is secured in a manner similar to that used at the other end. This procedure eliminates a projecting knot in the lumen of either vessel, and if the stitches are placed accurately and drawn taut throughout, they do not present unusually into the lumen of either vessel. The closure of the incision in the vein is effected by a continuous suture apposing the cut endothelial surfaces. The operation of Pearson, though entirely independent, is identical with that of the Matas-Bickham operation.

Of course, the ideal to be aimed at in these operations is the preservation of both vessels, especially when dealing with the large trunks at the root of the neck and limbs; but when for any technical reason, it is difficult or impossible to close the orifice of communication without sacrificing the vein, this should be done without hesitation if the sacrifice preserves the lumen of the artery or closes the fistula. In the cases he reports the vein is preserved in its integrity after a transvenous suture, while in others the vein was ligated above and below the anastomosis and in still others the vein was used by plication or as a reinforcing flap to protect the line of suture.

**Operative Removal of Embolus.** Sunneberg<sup>94</sup> reports another successful case to add to the 6 on record in which an embolus was removed from an artery with a permanent cure. These 6 are the only permanent cures from arteriotomy which he has compiled. The patient was a man of sixty-three. The common femoral artery was incised, the embolus drawn out, the spurting blood arrested by clamping above, and the artery sutured afterward with button sutures, which only pass through the outer and middle coats, avoiding the intima. The suture material was fine silk lubricated with petrolatum, and fine curved needles were employed.

**Fractures.** FRACTURES OF THE FEMUR. Jones,<sup>95</sup> in his address to the American College of Surgeons, said the lessons civilian surgeons should learn from all war surgery is clear. If such results as Bowdly has reported (page 286) can be obtained by such simple apparatus as the Thomas splint in compound war fractures, why should it be necessary to have recourse to more complicated methods? Why should the student be taught that fractures of the femur can be only adequately treated with plates and screws or other internal splintage? A further lesson has been that we have in the past underestimated the time necessary for bone to sufficiently consolidate to bear the body weight. This delay in solidification is still more pronounced in war wounds. After several months of apparent union, angulation may occur unless the bone is protected. Jones has found that the best protection is the caliper splint. He uses a Thomas splint which runs into the heel of the boot,

<sup>94</sup> Hygiea, Stockholm, January 16, 1920, No. 1, vol. lxxxii.

<sup>95</sup> Surgery, Gynecology and Obstetrics, January 20, 1920, No. 1, xxx, 7.

and he feels that it should be used in the later stages of the treatment of all fractures of the femur. The removal of the splint should be gradual, and the experiment should be made under careful observation.

A PORTABLE SUSPENSION FRAME EMPLOYED IN THE TREATMENT OF THE WOUND DURING THE EUROPEAN WAR. Lyle,<sup>96</sup> in a series of illustrations, shows the evolution of the overhead frame which was used in the treatment of compound fractures of the lower extremities. Its final form eventually became known as the American apparatus, though Lyle tells of its being made first at the Juilly Hospital of the American Ambulance. This was described in *PROGRESSIVE MEDICINE* last year, December, pages 284 to 287, and it is quite time that Lyle receives the credit for this apparatus. The frame differs very little from that described by Blake and Bulkley and reviewed last year, except for the addition of a hinged auxiliary to the Thomas splint for exercising the knee-joint. This was a later development and was in line with Blake's efforts to preserve the function of the limb by abandoning absolute fixation and substituting the principle of balanced suspension and traction, with the limb in the position of physiologic rest.

The advantages of this suspension frame in the treatment of injuries to the lower extremities are testified to by practically every surgeon who has served overseas in the base hospitals. It materially lightened the burden of nursing and was a decided factor in promoting the comfort and well-being of the wounded. One is compelled to confess a disappointment in not seeing a more general adoption of this apparatus in our civil hospitals. Its indications and uses are just the same in civil practice as in military practice, and if surgeons will make the proper effort, they will be able to convince the personnel of the civil hospitals and particularly the administrative part of their organization that it is not an unnecessary expense but a real economy to the patient, the nurse and the surgeons, and though it may be unsightly in a hospital ward, it is efficient far beyond such criticism.

THE TREATMENT OF FRACTURES BY SUSPENSION AND TRACTION is described by Blake<sup>97</sup> in a paper read before the American Medical Association.

The principles are based on the following facts: (1) In every fracture of a long bone, the proximal fragment tends to occupy a certain position, which is determined by the muscles attached to the fragment. The forces produced by the muscles may be termed intrinsic.

2. This position, which may be designated as the position of election or rest, is readily modified up to certain limits by any slight extrinsic force, that is, one operating from without.

3. Conversely, if a slight restraint is supplied, considerable motion at the proximal articulation may occur without there being any change in the absolute position occupied by the fragment.

4. Traction on the distal fragment not only prevents overriding and shortening, but, when applied in the direction of the axis of the proximal

<sup>96</sup> *Annals of Surgery*, June, 1920, No. 6, lxxi, 716.

<sup>97</sup> *Journal of the American Medical Association*, September 6, 1919, No. 10, lxxiii, 748.



fragment, when in the position of election or rest, also tends to prevent harmful angulation at the sight of the fracture as a consequence of the restraining action of the sheath of the stretched muscles about the proximal fragments.

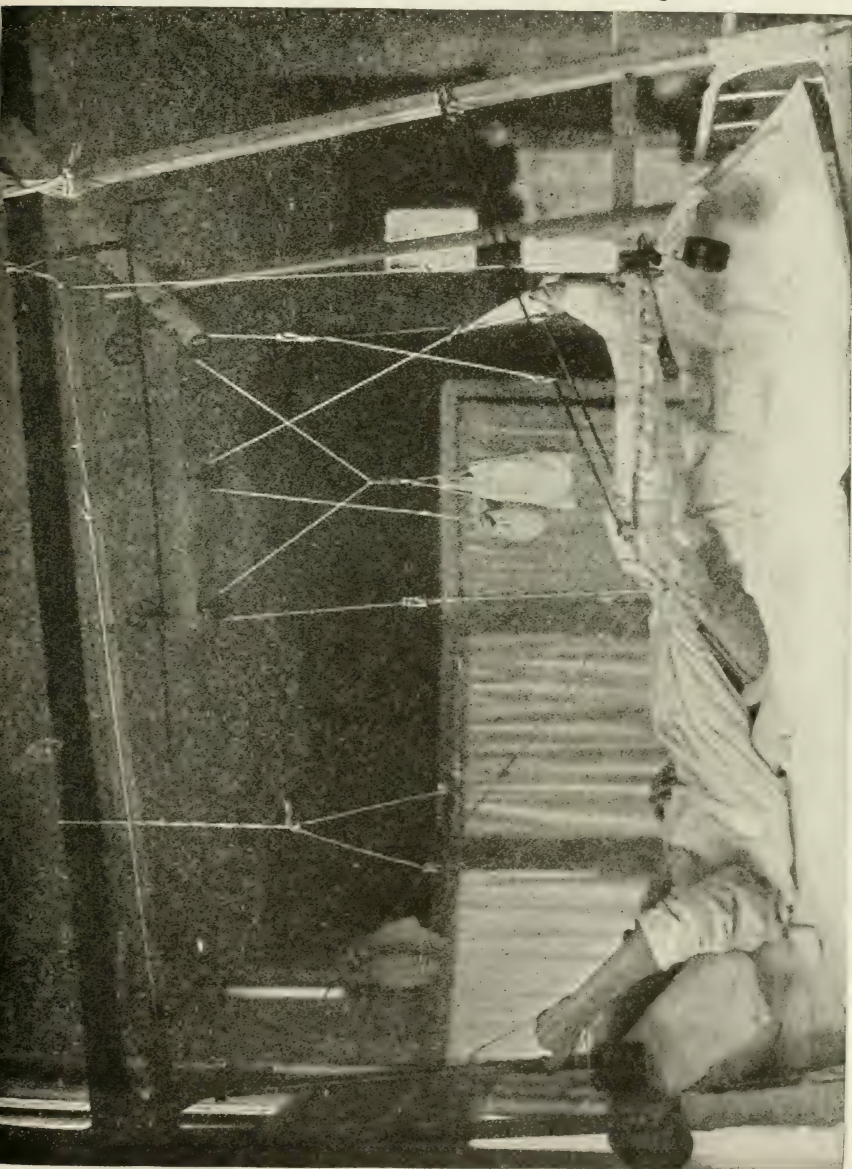


FIG. 70.—Intertrochanteric fracture of the femur in a patient, aged eighty-three years. Treated by the balanced suspension and traction method. Splint (Thomas), with hinged auxiliary for exercising the knee-joint. Traction by adhesive bands and divided pulley and weight extension. The patient is seen grasping one of the divisions of the extension. The other weight is seen close to the foot-piece of the hinged auxiliary splint. By pulling at the head of the bed the patient can exercise the leg at the knee. The patient obtained a firm, long union without shortening and left the hospital walking on a caliper splint. (Lytle.)

5. Proper counterbalanced suspension, by allowing the limb to follow the body, permits a considerable latitude of movement of the latter in bed without deranging the relative position of the fragments.



6. Traction, in order to accommodate itself to the position of the patient (unless the traction is contained within the splint), must be made by a weight and cord running on a pulley; and the pulley should

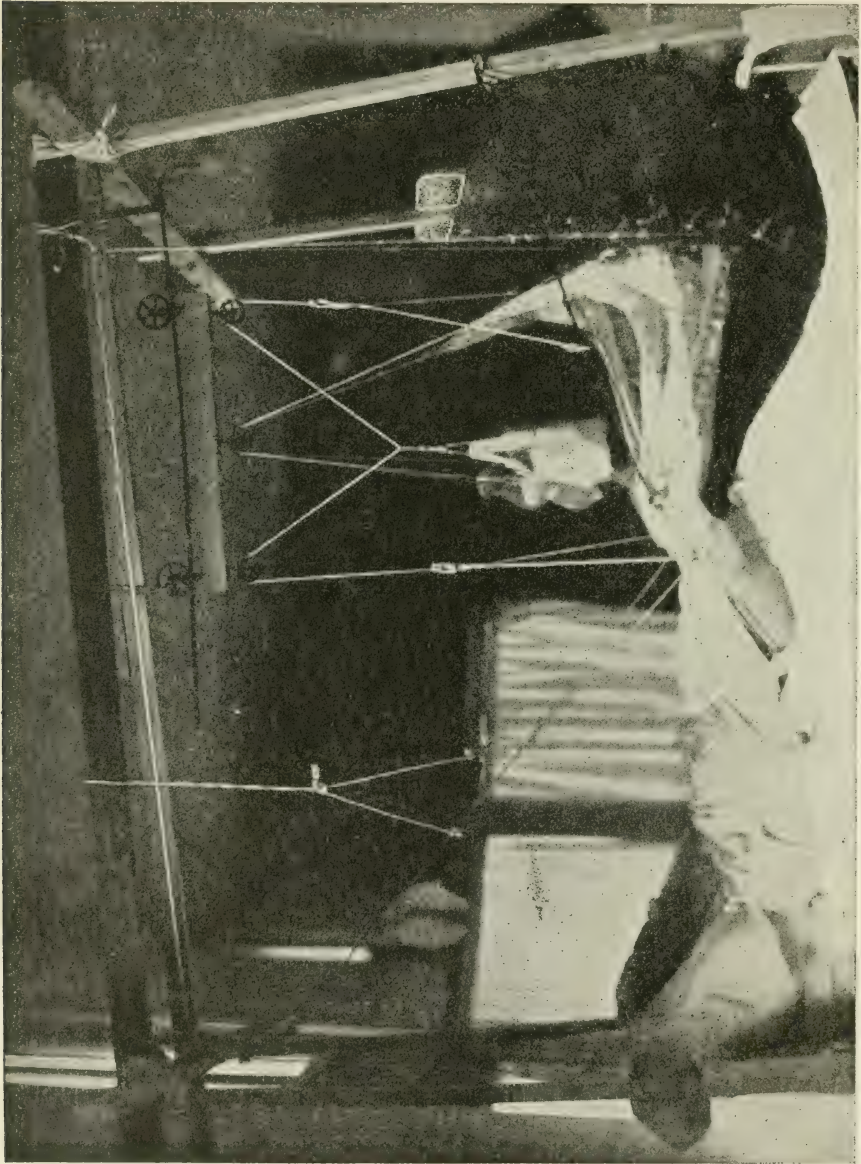


FIG. 71.—Same patient. Superimposed picture to show the range of movement. (Lyle.)

be as far as possible from the point at which traction is made so as not to limit the swinging of the limb.

7. The lack of fixation in permitting a certain amount of motion between the fragments does not delay union; on the contrary, consolidation appears to be more rapid, probably because of better nutrition.

8. In fractures of the humerus and femur, in both of which fixation of the proximal fragment is impossible, the limb being free to follow the movements of the trunk, no evident angulating strains occur at the site of the fracture, and commencing union rapidly affords the slight restraint necessary to maintain the fragments in position.

9. With traction and suspension properly applied, it is possible to move all the joints of the fractured limb throughout the treatment, no matter which bone is fractured.

The principles of the treatment are, to avoid actual fixation; to employ traction to its fullest possibilities in overcoming deformity, and to use suspension so as to afford the greatest freedom of movement, both of the trunk and of the joints. The chief and underlying principle is conservation of function.

UNUNITED FRACTURES OF THE HIP. Henderson,<sup>98</sup> in a review of 120 cases of ununited fracture of the hip, found that in the majority the non-union was a result of an incorrect diagnosis at the time of the accident and that, in the minority, even when the proper diagnosis had been made, no treatment had been carried out; often, it is true, for some justifiable reason. It was surprising how frequently elderly persons, who, after a severe fall and disability on account of intense pain in the hip, were told, without being examined, that they were suffering from a strain. In none of the cases in his series was there a history of really proper treatment for the fracture. As a group, ununited fractures of the hip offer a comparatively small percentage that are suitable for surgery: Of his group, 21 per cent. of the 120 patients were considered suitable for operation. In 38 per cent. the operations were successful, giving, however, for the entire group of 120, only 8.3 successfully treated. Advanced age, poor general health are contra-indications to operations, but the chief indication is absorption of the neck of the femur. A person of twenty-five years may in five months after the accident show so much absorption of the neck of the femur that none of the measures herein considered offer any hope. Any means, in suitable cases, that will freshen the fractured surfaces and maintain them in apposition, is sufficient, but autogenous bone pegs are the most ideal. From their experience, the fibula seems to be the best piece of bone to be used; it is easily obtained, and is never missed by the patient if taken from anywhere four inches above the external malleolus.

RECONSTRUCTION AND AFTER-CARE OF OLD, UNREDUCED POTT'S FRACTURES. Sneed<sup>99</sup> states that the most frequent disability following in the wake of Pott's fractures is flat-foot. This is often exaggerated and rendered painful and persistent by a slight posterior displacement of the foot on the tibia or a widening of the ankle-joint, due to a rupture of the tibiofibular ligament. There is another factor in the production of flat-foot which is inexcusable and that is in the fixation of the foot at right angles, but in a position of valgus, in which the muscles supporting the arch of the foot are put on a stretch. When the patient is allowed

<sup>98</sup> Surgery, Gynecology and Obstetrics, February, 1920, No. 2, xxx, 145.

<sup>99</sup> Journal of the American Medical Association, November 1, 1919, No. 18, lxxiii, 1342.



to walk in the support with the foot in this faulty position, the flat-foot develops which is largely the result of a loss of muscle tone.

The *treatment* of these cases varies with the condition that is present and with the end-results that are desired. The operative procedure in the case illustrated consisted in the manual forcing and overcorrection of the position of valgus into that of varus, and also of manually correcting the pes planus. An incision was then made over the internal malleolus, the fibrous tissue removed, and the ends of the fragments freshened by chiseling. An inlay of bone was then slid down from the tibia into a groove prepared in the malleoli and this was sutured into place. Third, an incision was made over the fibula and the fibula divided transversely about one inch above the ankle-joint; with a curette the fibrous tissue, with the periosteum, was removed from between the tibia and the fibula from the ankle-joint up to the line of fracture. Fourth, the tendon of Achilles was divided by the "Z" method, and the foot was forced up into dorsal flexion. This reduced the posterior displacement. The foot was then pulled around into slight varus approximating the fracture of the external malleolus to the tibia and forcing the raw surfaces of the tibia and fibula together. The wounds were then closed without drainage.

The foot was put up in plaster of Paris in the corrected position and a redressing maintained for six weeks. An x-ray taken at this time revealed a reestablishment of the mortise in the ankle-joint as a result of union of the tibia and fibula, the union of the internal malleolus and an all around reconstruction of the bony anatomy of the foot.

*After-care.* The after-care consisted of: (1) Continual support which consisted of plaster of Paris for eight more weeks, then adhesive plaster strapping for two or three weeks longer, and, finally, a Whitman arch support with a raise of the shoe of one-quarter inch on the inner border of the heel and toe. The exercises and manipulations were those for reestablishing muscular power of weak feet in general.

A NEW AND EFFICIENT METHOD FOR THE USE OF WIRE IN THE SURGERY OF BONE. The use of wire in the surgery of bones has a limited field but it is a very definite one, for no other method is practical in some cases. Neff and O'Malley<sup>100</sup> hold that the indications for the use of wire are as follows:

1. The holding of any small fragment in apposition with a larger fragment where it cannot be done by the closed method; for instance, (a) a short lower end of the radius displaced forward and upward, and where the flexors act strongly and overcome the extensors; (b) the holding in position of bone fragment in comminuted fractures, such as of the lower end of the humerus, where it is essential that these fragments be held in place and remain so until union takes place. They do not advocate it in fractures of the long bones, where very strong support is needed to hold the fragments in apposition, as in the shaft of the humerus, femur, tibia, or both bones of the forearm.

In describing their technic, the only peculiar part of the procedure is the preparation of the wire. Silver or copper wire of a proper gauge is

<sup>100</sup> Surgery, Gynecology and Obstetrics, June, 1920, No. 6, xxx, 612.



selected. The wire is drawn straight by traction on each end and passed through the blue flame of a Bunsen burner in order to burn off any grease that may be present. While it is kept on tension it is rubbed over with liquified zinc chloride on an applicator. The prepared and heated

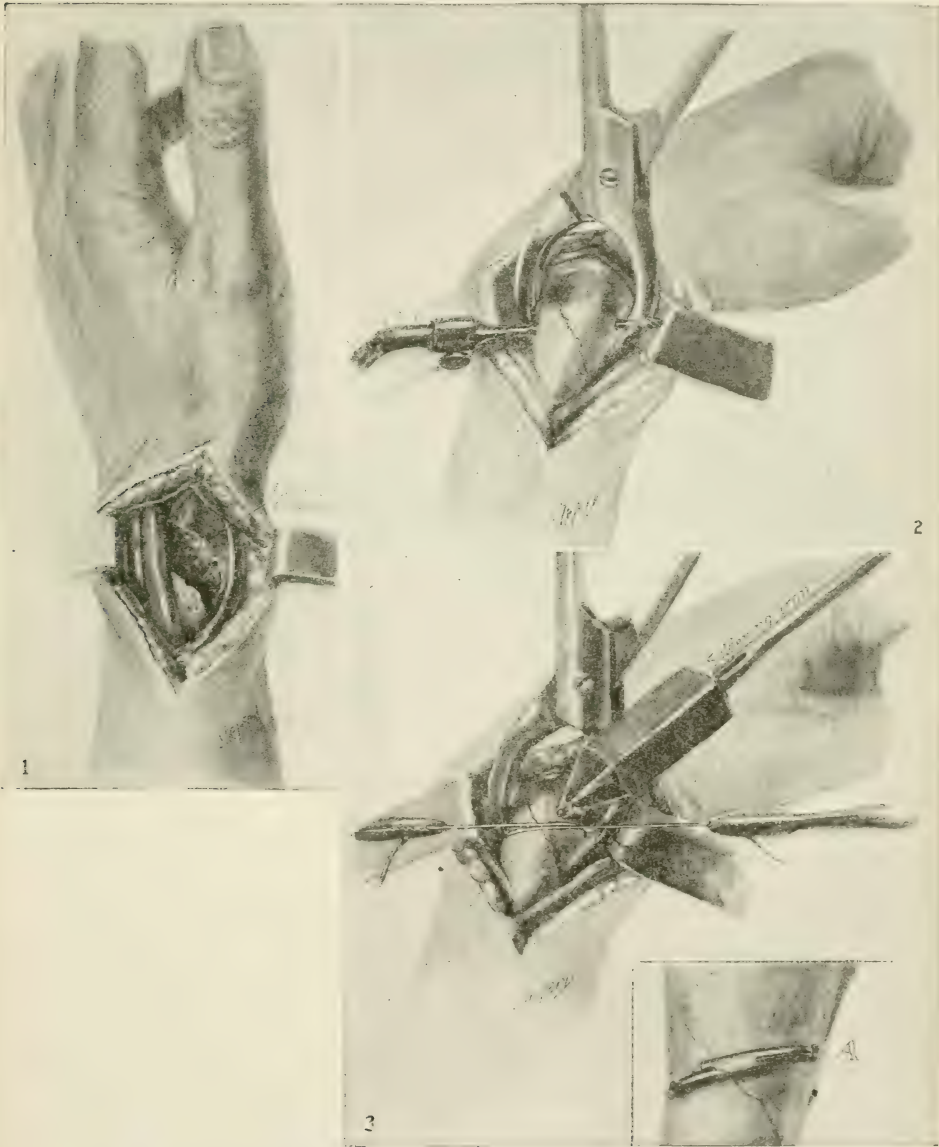


FIG. 72.—Incision to bone, showing fracture and exterior tendons. (Neff and O'Malley.)

FIG. 73.—Fragment held in place with drill going through bone at joint of greatest density. (Neff and O'Malley.)

FIG. 74.—Fragments in place with wire through dull hole ready for soldering. Insert *a*, fragments united with soldered wire in place. (Neff and O'Malley.)

soldering iron carrying a small drop of solder is now passed over the entire length of the wire and around its circumference. This will cause a thin film of solder to adhere to the wire as it did to the iron. While the wire and solder are still hot they may be wiped over with clean, dry gauze to carry away any excess of solder and leave a smooth surface. The wire should be boiled with the instruments before being used. The iron is used during the operation by wrapping the handle in a sterile towel as in the use of the cautery.

**GUNSHOT FRACTURES OF THE FEMUR.** Bowldy,<sup>101</sup> in the paper presented before the clinical congress of The American College of Surgery, reported the principles upon which gunshot fracture of the femur were based in the British Army, and it is quoted in its entirety, for the R. A. M. C. have had unprecedented experience in the treatment of this type of fracture during the war.

1. The first general principle that was universally adopted was that the apparatus employed should be a skeleton metal splint, and that this should be used so as to enable traction to be applied, either directly downward in the direction of the long axis of the bone, or else in various degrees of abduction or flexion. This is the essential foundation upon which all else is based.

2. The direction of the traction and the amount of flexion or abduction required were guided throughout by frequent roentgenograms. These were always taken by a portable *x*-ray apparatus brought to the side of the bed and, by the aid of the *x*-ray, the position of fragment was altered, so as to obtain accurate apposition. Without the frequent use of *x*-rays at the bedside, it is not possible to obtain uniformly good results.

3. The length of the limb was first measured daily and afterward less frequently, and it was found most useful to keep a "Chart of Shortening" (or lengthening) over the patient's bed. It became a custom to apply extension until the injured limb was definitely longer than its fellow, as it was found that this gave the best end-results. It is more important to bear in mind that, even when the main fragments of bone are separated by an interval of one or two inches, the gap can be completely filled by a new bone.

4. "Fixed" extension proved to be not so good as "Continuous" extension. The traction can be employed by either fixing the foot and then lifting the end of the bed and letting the weight of the patient act as the extending agent, or else by applying weight traction. On the whole, they found the use of the patient's own weight was the method most in favor.

5. Movements of the knee-joint were begun early, and slight flexion of the knee was always preferred to traction on the fully extended limb. The early experience in the war had produced a very large proportion of permanently stiff knee-joints in this type of fracture. This might be due to (a) mild sepsis, (b) fracture near the articulation, (c) loss of elasticity and scarring (and adhesions of muscle, tendons and skin).

<sup>101</sup> Surgery, Gynecology and Obstetrics, February, 1920, No. 2, xxx, 135.

The attachment of an auxiliary splint to the main Thomas splint enabled the knee to be freely moved or fixed at any angle of flexion. Bowldy credits Beasley for devising the calipers which were originally suggested by Ransohoff, Cincinnati.<sup>102</sup> They were especially valuable for cases of fracture of the lower third of the femur, for their use completely overcame the flexion in these cases, and they also enabled the knee-joint to be freely moved without disturbing the traction on the femur. He suggests that if calipers are to be employed, the following precautions are necessary. [The reviewer can, from personal experience, emphasize these precautions.]

(a) Rigorous asepsis, (b) avoidance of the synovial membrane, (c) avoidance of the thin articular bone of the condyles by fixing the calipers on the denser bone at the level of the abductor tubercle, (d) the use of any simple method for preventing the too deep penetration of the bone by the points of the calipers.

6. For fractures of the upper third and the neck, he advocates placing the patient upon a special segmented mattress that has been described by Major Pearson.

7. When union was sufficiently advanced, patients were gotten out of bed and the length of a limb maintained by the application of "walking caliper splints" fixed to the heel of the boot. If these were employed, the use of the limb undoubtedly accelerated the formation of callus, but if they were not provided, many limbs yielded and became bowed in attempts to walk.

8. In the treatment of the wounds, delayed primary suture or secondary suture gave the best results. Cases so treated showed a more rapid union of the fracture and a great shortening of the febrile period. They were also much less liable to necrosis of fragments and to secondary abscess. The natural result was a decreased mortality in sutured cases as compared to those unsutured and a great diminution in the amputation rate. In those cases which could not be sutured, the period of separation was often shortened by the employment of the Carrel method.

9. The question of the removal of bone was not entirely settled when the war ended. There is no doubt of the advisability of removing badly smashed fragments which have been completely separated. But, while most surgeons did not advocate the removal of more than this, some operators followed the advice of Leriche and practised "subperiosteal" removal of many of the partially attached fragments. There seems no doubt that on the one hand the removal of all fragments which are liable to necrose hastens the healing of the wound, while, on the other hand, this removal delays the union of the fracture and in the opinion of some very competent observers, has been responsible for permanent non-union in many instances.

*Amputations.* In the amputations performed to save life in compound fractures of the femur, in one-third of the cases it failed. About 20 per cent. of all patients with fracture of the femur lost their limb either by primary or secondary amputation.



At the front the most common cause for amputation was the extent and severity of the injury which rendered it impossible to save the limb. Laceration of the vessels and gas gangrene were two other indications.

Many lives were saved by the employment of blood transfusion and the use of gas and oxygen as an anesthetic.

*Final Results.* 1. *Shortening.* The methods of treatment of 1918 (just described) guarantee that unless there has been very extensive loss of bone, no shortening need appear. Even if one or two inches have been destroyed, the gap can be filled with new bone, and there is no objection to maintaining the fractured ends in full extension. It had formerly been the practice of some surgeons to allow the separated fragments to come together so as to promote union, but this is to be condemned.

Practical experience has shown that it is more difficult to obtain a full length limb in cases of simple fracture, such as occur in civil practice, for the uninjured muscles offer far greater resistance than those in a limb wounded by shell or bullet, and consequently more extension is required. Statistics show that the majority of patients recover without any shortening and that in only about 5 per cent. of all patients was there more than one inch of shortening. When this is compared with Tuffier's report to the Interallied Conference in 1917,<sup>103</sup> in which shortening was constant in every case of the group of 16,392 cases reported and varied from 1 to 20 cm. and in 22.42 per cent. there was absolute functional loss of the extremity, one can realize the advances that were made in the treatment of this condition.

2. *Malposition.* The common displacement is the falling back of the lower fragment. The difficulties of correcting malposition almost disappeared in France as soon as a full length of the limb could be secured. A small percentage of fractures near the knee and hip recover with some small displacement, but at least 80 per cent. of the whole group of cases recovered with good position. In fractures of the shaft, good position can practically always be secured, but it is most important to support the bone at the site of the fracture so that the natural anterior curve of the femur is maintained or even slightly exaggerated.

3. *Stiffness of the Knee-joint.* There is no doubt when precautions are taken during treatment, stiff knees in cases of fracture of the shaft of the femur should be very few. Of 264 cases, Major Stout reports the average of flexion of the knee was 43 degrees. Again compare this to Tuffier's report, in which he found ankylosis or stiffness of the hip, knee or ankle in 76.2 per cent.

4. *Stiffness of the Hip-joint.* This has not been a frequent complication and it should never occur except in cases where the fracture either involves the neck of the bone or the trochanters.

5. *Stiffness of the Ankle-joint.* This can always be avoided if care is taken not to keep the foot cramped by bandages, and to allow and encourage daily movement at this joint.

<sup>103</sup> PROGRESSIVE MEDICINE, December, 1919, p. 294.

6. *Sinuses and Necrosis.* Sinuses will not occur unless necrosis is present. The early closure of the wound and the more prompt removal of sequestra than in former years has greatly diminished the number of sinuses.

7. *Non-union.* This is decidedly rare, and did not occur in more than 1 per cent. of the cases retained in France.

**Treatment of Non-union and Compound Fractures.** DeForest Willard<sup>104</sup> reports the method used in the R. A. M. C. at the Military Orthopedic Hospital at Shepherds Bush and at St. Kathryn's Hospital, London. These were British casualties that needed reconstruction and were old cases, some dating back to the 1915 campaign. He felt that more skilful débridement, with careful preservation of all possible fragments with attached periosteum, and the accurate and prolonged maintenance of proper alignment, as with the Thomas splint, were the main factors in a marked decrease in the percentage of non-union in the compound fractures of the later years of the war, particularly in the 1918 campaign.

The causes of non-union were: (1) infection; (2) extensive loss of bone substance caused either by the missile or by over enthusiastic removal of bone fragments at the primary operation; (3) imperfect fixation.

The treatment of the cases divided itself into two distinct parts (1) the restoration of function of the disabled limbs, and (2) the treatment of the fracture itself. Both parts of the treatment are equally important, but the monotonous time-consuming functional restoration is often neglected because of our interest in the treatment of the fracture. Infected fractures of the arm and forearm provided the best examples. Finger motion, with pronation and supination, were almost invariably lost in these cases, and it was with the utmost difficulty that functional efficiency was attained. Manipulation under an anesthetic seemed to increase, rather than decrease, the disability. Prolonged treatment with splints, with gradually forced motion combined with hot baths and massage gave the best results. If this part of the treatment is delayed until after bony union is established, free motion of the joints distal to the fracture is almost impossible to obtain and, from the patient's standpoint, his hospital care is valueless because the restoration of motion is the goal for which he is aiming. Much of this disability can be avoided by early exercise—active whenever possible, passive only when the fracture is so low that active motion is prohibited.

During the preoperative period, in ununited fracture, systemic conditions should be corrected, the general nutrition of the limb improved by massage and hot bath treatment; incidentally heavy massage may be of great value in determining whether or not the scarred tissue in an old infected area is permanently healed, for if a scar can withstand heavy manipulation, it is safe that the operative procedures will not reawaken the infection. In mild infections, six months is sufficient time to elapse before considering operation. In severe infections, nine to twelve months should elapse. Just before operation, a ten-day course of heavy

<sup>104</sup> *Annals of Surgery*, February, 1920, No. 2, vol. lxxx.



massage of the scar should be carried out to determine the amount of reaction.

At the operation the scar tissue was dissected away both from the soft parts and from the bone fragments. Smears were made from the deep tissues and the wound closed. If the infection was reawakened, as it was in a moderate percentage of cases, the wound was widely opened and sterilized with Dakin's solution. When the bacteriological report was negative for streptococci and the wound remained closed, or had become sterilized with the Dakin's solution, the second operation was done, usually within eight or ten days. The second operation consisted in the actual repair of the fracture. No one procedure was found applicable in all cases, but the simpler the operation, the better the result. If apposition could be maintained with catgut or kangaroo tendon, no more elaborate procedure should be attempted. In selecting the materials for internal fixation, it must be remembered that these infected wounds have not the resistance of simple fractures. He objects to the use of metals of all form, but approves of autogenous bone grafts, especially when there is a gap to be bridged. Though theoretically the sliding type of graft is the best, a graft taken from healthy bone is always preferable, because, to be successful, a graft should be snugly imbedded for a considerable distance into healthy bone in both fragments, it should reach into the medullary cavity, it should preserve both its periosteum and endosteum, and it should be healthy, non-sclerosed bone throughout its whole length. It is difficult to fulfill all of these conditions with a sliding graft in an ununited fracture.

PROJECTILE FRACTURES OF THE LONG BONES. Speed<sup>105</sup> points out that to understand the mechanism of fractures of long bones, one must appreciate their physical properties, elasticity, strength and toughness, and realize that these properties are governed by the same physical laws as similar supporting substances when they are subjected to stress and strain. In long bones the hard shell or cortex is intended to furnish rigidity and form, while the cancellous inner and terminal portions possess much greater strength to resist forces applied at any given point in the normal axis of the supporting trabeculae. Thus when the condyles of the femur or the os calcis are subjected to forces in the normal direction of their weight-bearing or muscle pull, this cancellous bone will withstand enormous pressures. In civil accidents the body is subjected to direct trauma, and the stresses are two main types, compressional and torsional.

A compression force operating against a long bone not only has a crushing effect upon the surface nearest to the force applied but, at a point directly opposite, this same power is attempting to tear apart the distal surface. Thus it is being subjected to a compression force at one point and a tearing force on the opposite surface. It has been found experimentally that the ratio of a compressional force to a *tensile force* is as three to two; consequently, when subjected to these forces, a bone gives way first from the tensile force, especially when there is a relatively slow acting force. The planes<sup>106</sup> of cleavage as shown in the diagram

<sup>105</sup> *Annals of Surgery*, April, 1920, No. 4, lxxi, 493.

<sup>106</sup> *Ibid.*, 1920, lxxi, 594.



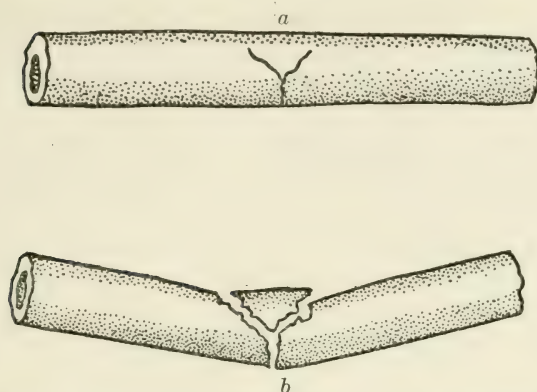


FIG. 75.—*a*, Diagrammatic compression fracture; the bone starts to give on the tensile sides; planes of separation diverge as it bends; *b*, resulting fracture with triangular-shaped pieces broken out on compression side. (Speed.)

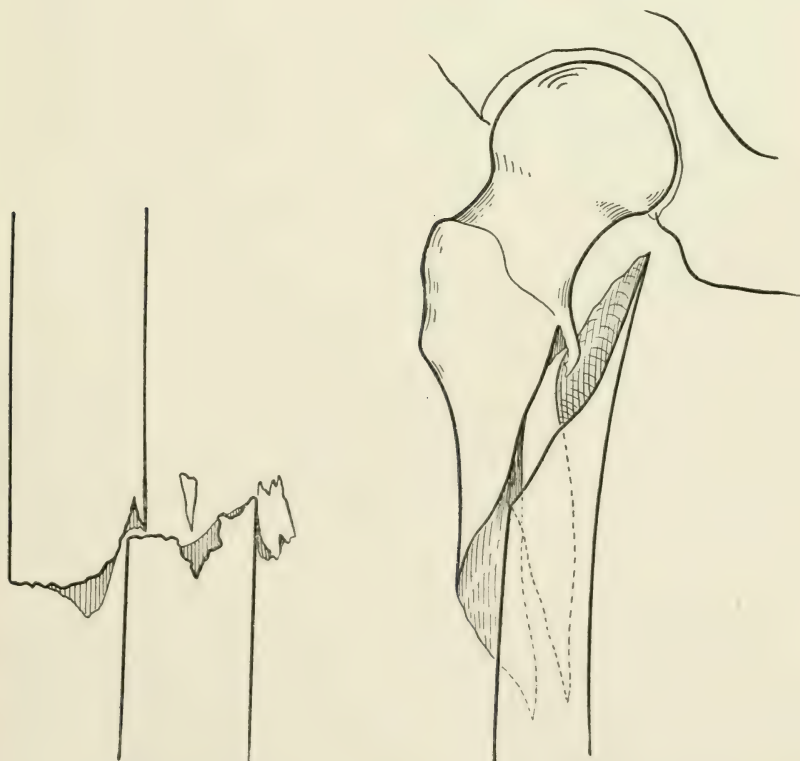


FIG. 76.—Compression fracture of femur a quickly acting ponderous force, with almost transverse fracture. Skiagram tracing. (Speed.)

FIG. 77.—Skiagram tracing spiral fracture of the femur from torsion violence. A glance at a skiagram is sufficient to differentiate the two general types of fractures, (Speed.)

(Fig. 75), start on the tensile side, that is, the convex side of the bending bone, and at a point opposite the compression point. The bone being somewhat elastic is bent slightly out of its long axis and, in giving way, arches more and more, so that these plains of separation tend to assume an oblique direction. Thus we see the breaking out of a triangular-shaped piece of bone on the side of the compression. Only when the compression force is great enough to overcome the bone instantly do we get a transverse line of fracture, the so-called shearing fracture. Any force of less power and of slower action invariably results in an oblique fracture. If the compression is in the longitudinal axis of the bone we get the same resulting break, or, more rarely, longitudinal cracks running up the long axis. Buckling and green stick fractures are also examples of compression fractures.

The second common force in fracture is torsional violence, which results from twisting and affects particularly bones of the extremities. This causes spiral fractures. We find these fractures in the arm and leg when the limb is twisted in being caught in falls or when the body is twisted with the limb fixed. Usually spiral fracture of the leg is caused by the foot being turned violently outward, as in slipping or catching against an object. So regular is this mechanism and so universal the out-turning of the foot that we can say that spiral fractures of the right leg are left-handed while those of the left leg are right-handed. When torsional violence of sufficient power to cause fracture is applied to a long bone, which may be compared to a cylinder, it starts to give at some point on its surface and unrolls in its continuity. The sharp pointed ends of the fragments are found on the same surface of the bone.

Other fractures frequently enter into the physics of compression or spiral fractures, which result in more or less complicated lines of cleavage.

When a long bone is struck by a bullet or other penetrating foreign body, the bone is subjected at that point to a compressional violence of varying degree depending on the momentum of the projectile. If struck squarely without any inclination, we would expect that the resulting fracture would appear much as a compression fracture in civil life. It does. There is the same oblique or transverse plane of bone separation with frequently a triangular portion broken out on the tension side. This is particularly true if the projectile's velocity has not been great, and the total force offered has not been sufficient to cause a break. If the projectile has had a very high velocity it may act, as in the case of a conical-nosed bullet, over a very small area, causing puncture, and passing clean through the shaft of a long bone leaving a track but causing no complete fracture. No gunshot fracture then, unless complicated by other forces, could be a spiral fracture and none of them are. The falling of a man simultaneously with the receipt of a gunshot fracture might twist the limb to produce a spiral fracture, but this rarely happens. Thus gunshot or projectile fracture is merely a compression fracture with usually a wide displacement of the loosened fragments. The dimensions of the fragments in gunshot are inversely proportional to the velocity of the projectile. The less the velocity of the projectile, the larger the adherent fragments and the smaller their number, while with a high

velocity projectile there are fewer adherent fragments, and a much larger number of them and they are widely scattered in the track of the projectile, even penetrating into the surrounding soft parts.

**NECROSIS FOLLOWING COMPOUND FRACTURE.** One of the war legacies that surgeons are encountering at the present time is the problem of bone necrosis following compound fracture. The surgical treatment of old fractures of the long bones with osteitis of the periosteal callus presents real technical difficulties. It does not suffice to remove the sequestra, or to abrade the necrotic surfaces or even to curette all

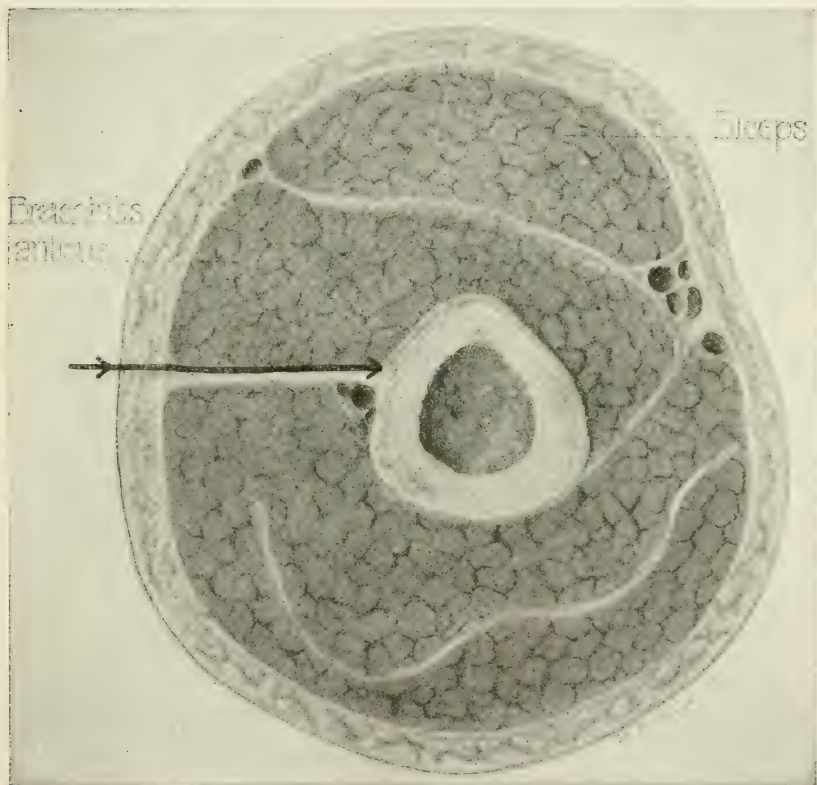


FIG. 78.—Line of access to the humerus. Right arm, upper surface. (Loewey.)

the foci of osteitis—this form of surgery, which has been practiced on thousands of cases, since the beginning of the war and before it, has usually resulted in failures. Such operations produce only irritation of the periosteum and a new formation of pathological callus. Nothing short of a radical operation is adequate. All the spongy tissue affected with osteitis is removed subperiosteally. In these old fractures, seen after the period of consolidation, the medullary canal is always closed, either by a plug of bony or fibrous tissue. Loewey<sup>107</sup> says that this medul-

<sup>107</sup> International Clinics, Series 29, i, 170.



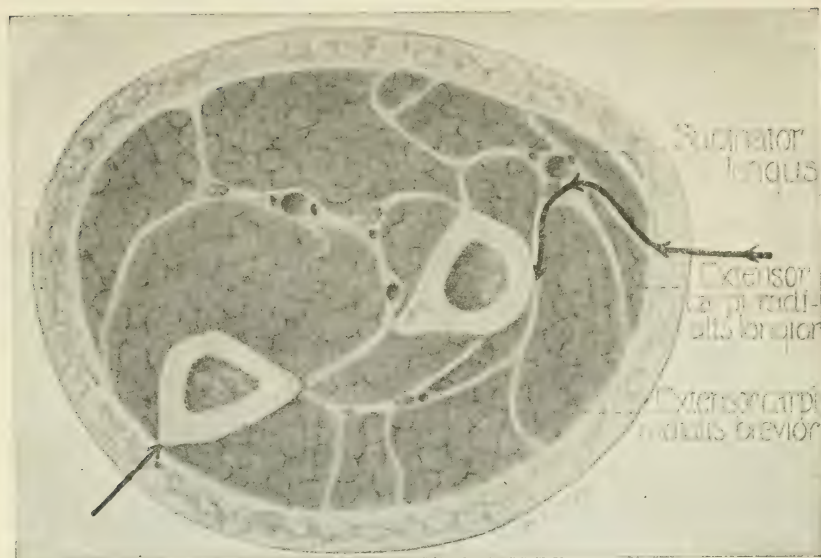


FIG. 79.—Line of access to the radius and ulna. Left forearm, upper surface. (Loewey.)

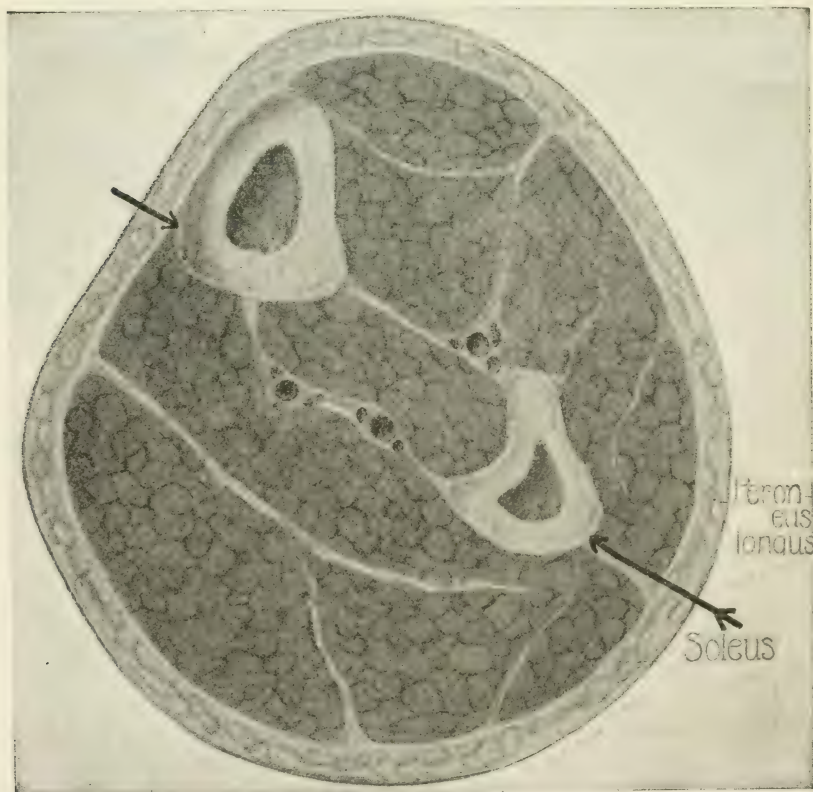


FIG. 80.—Line of access to the tibia and the fibula. Left leg, upper surface. (Loewey.)

lary plug should never be removed. No bony cavity which cannot be filled by the healing of the soft parts should be left. All overhanging walls must be removed with a chisel to make possible the apposition of the collapsing soft parts to fill in the bony defects. All tunnels in bone should be converted into trench-like excavations by removing the roof.

**Osteomyelitis.** Babcock<sup>108</sup> reports a new method for the immediate sterilization and closure of chronic infected wounds of the soft tissues and bone which in a paper he read before the American Medical Association. In the foreword he makes the rather unfortunate statement "with the mass of chronic infections of the war the aim of the Carrel-Dakin treatment—the early closure of the wound—has not been attained." Few of the soft tissue wounds, and I dare say less than 1 per cent. of the thousands of bone infections returned from overseas, have been brought to an aseptic suture. Despite the widespread use of the surgical solution of chlorinated soda (Dakin's solution) and the presence of officers especially trained in its use, some of our large army hospitals could not, up to May 1, 1919, show even a single case of aseptic operative closure for osteomyelitis. "A treatment successful in the hands of highly skilled enthusiasts may fail in routine use when it exacts infinite care as to detail over prolonged periods of time and when it is adapted only to selected cases. It requires repeated operations and multiple, and, at times, exceedingly painful, dressings. The average surgeon is not constituted to stand on tiptoe all the time, his technic is not invariably perfect and his soul rebels against the constant infliction of pain. It is not strange, therefore, that he has so often failed in his Carrel-Dakin treatment." This series of statements is quoted verbatim. So many surgeons at the present time, as a result of their training at the Rockefeller Institute, the various army courses of special instruction, and their personal experience with the Carrel-Dakin method of sterilizing traumatic wounds for the primary, delayed primary, and secondary closure, are convinced of the possibilities of this method. Such statements, or the reviewer's criticism of them, will have little influence. There is some truth in each of these claims of Babcock's, but all of them are more or less exaggerated, and we feel sure that his statement of the aseptic suture of less than 1 per cent. of the bone infections returned successful from overseas will not be confirmed by the statistics of the U. S. A. M. C. The method which he offers as a substitute we refer to with the definite purpose of offering a warning. Briefly, it consists of the forcible injection into the sinuses of the chronic infection, a saturated solution of zinc chloride containing an alcoholic solution of methylene blue.

	Gms. or c.c.
Saturated alcoholic solution of methylene blue . . . . .	20
Caustic potash . . . . .	3
Phenol . . . . .	5
Ether (to make) . . . . .	100

As a result of these injections, there is a sterilization and devitalization of the infected tissues. If a section is made of the sinuses, it is found that the methylene blue has penetrated to a depth of 1 to 3 mm. Outside

<sup>108</sup> Journal of the American Medical Association, May 8, 1920, No. 79, lxxiv, 1301.

of this is a much wider zone of avascular, grayish-white tissue that has been sterilized and devitalized by the zinc chloride. The diseased area, which is fully included in the tissue which has been destroyed and stained by this antiseptic staining solution, is completely excised. If possible, all soft tissues and bones should be removed to a distance of at least 1 cm. beyond the blue coloration.

The use of a staining in débridement solution was employed more or less frequently abroad, brilliant green being the one of common choice and this rule of wide excision was found to be necessary. His other suggestions about the excision of scars, the destruction of bone cavities so as to obliterate overhanging edges, and the excision of multiple sinuses has been generally accepted by all surgeons. The original feature, however, the use of zinc chloride, has been abandoned for a long time by surgeons because of its power of massive destruction of the tissues and the difficulty of controlling its action.

In his closing paragraph, Babcock states that, "unless the surgeon can prevent the entrance of the zinc chloride into the general circulation during, and for five minutes after, the injection, and unless he is able to excise freely all chlorided tissue adjacent to important structure, he should not employ this method." The experience of others with this method would seem to demonstrate that this condition is a difficult one to obtain. Babcock speaks only of one death in his own experience. Three occurred at Fox Hills Hospital and another has occurred in Philadelphia, so that in offering as a substitute for the Carrel-Dakin treatment in the sterilization of chronically infected wounds (from which no deaths have directly resulted from the method) another procedure from which at least five deaths have directly resulted, a word of caution is certainly necessary.

Hyman,<sup>109</sup> commenting upon Babcock's report, feels that he has treated altogether too briefly the danger in the use of this method, and has not sufficiently emphasized the caustic properties of a saturated solution of zinc chloride upon the walls of bloodvessels. It is a powerful caustic reagent, capable of deep penetration, producing an eschar, and, if brought in contact with a large artery or vein, as the femoral vessels, may cause a sudden profuse secondary hemorrhage which can only be controlled by ligation (in continuity). In August, 1919, this method of introducing zinc chloride throughout the fistulous tract was practically abandoned at Fort McPherson for this very reason. He believes that it is a mistake to recommend the method to any one who does not realize the danger, without making due emphasis on what one may expect. The patient must be kept under careful observation after operation for at least ten days, since instances of severe hemorrhage have occurred many days after operation. The Surgeon-General's office in investigating the deaths which occurred following this procedure found, in several of the autopsies, zinc chloride in the liver. The result of this investigation of the army hospitals was that the procedure was officially discouraged.

<sup>109</sup> Journal of the American Medical Association, June 12, 1920, No. 24, lxxiv, 1663.



VACCINE THERAPY IN OSTEOMYELITIS. Tuffier, in a verbal communication during his recent visit to America at the meeting of the American Surgical Association, referred to the vaccine therapy in osteomyelitis. He said that it had been so uniformly successful that he had practically found it unnecessary to treat it by surgical measures.

Gregorie<sup>110</sup> refers to its use in acute staphylococcus osteomyelitis, and describes 8 cases in infants and older children in which he used a stock staphylococcus vaccine until the autogenous vaccine was ready, so as to waste no time. This proved so effectual that in some of the cases the stock vaccine was continued to a complete cure. The dose seemed to be important: Starting with 200 million of the killed microorganisms, and giving from 2 to 7 injections, the intervals being guided by the reaction of the heart and kidneys. The pulse is usually high in eight to ten hours, and continues so for two or three days.

**The Treatment of Bone Cavities in Close Proximity to the Joint.** Bone cavities in close proximity of joints do not permit of sufficient removal of the roof and side walls to allow the desired collapse of the adjacent soft tissues. Martin<sup>111</sup> calls attention to the work of Chapet, 1903, and Calforia, 1918, in whose experiments fat transplanted into bone cavities of animals was found to be completely replaced by newly formed osteotic tissue. X-ray examination of fat transplanted into bone in man show apparently a similar result. It has certain obvious advantages for the plugging of wound cavities. It does not readily support bacterial life, nor does it readily undergo the decomposition. Moreover, when fat is broken down by the enzymes of bacteria, it probably splits into fatty acids or their salts (soaps) and glycerine, none of which are especially harmful to the tissue. The fat seems to be easily taken out by the body cells and appears to have physical properties suitable for the healing of the overlying skin. Martin offers the following conclusion with regard to the treatment of infected bone cavities:

1. The complete removal of all the infected bone lining the cavity, all foreign bodies, and every particle of dead bone, is essential.

2. In the majority of cases the cavity must be obliterated to ensure healing. This is accomplished most satisfactorily by removing a sufficient amount of the wall of the cavity to allow the soft parts to fall in and fill it up.

3. In certain tunnels in bone and cavities near the joints, some form of plugging may be indicated and of the many materials used as plugs, three fat transplants present obvious advantages. The two-stage operation, with careful sterilization of the cavity, by the Carrel-Dakin technic, is of great value.

4. The preparation of the wound consists of the excision of the skin about the margin of the cavity and the freeing of it from the underlying tissues until its edges can be approximated without tension. Exact hemostasis of the soft parts is essential.

A piece of fat distinctly larger than the cavity to be filled should then be excised from the abdominal wall and thrust into the cavity, the end

<sup>110</sup> Paris médicale, October 11, 1919, No. 41, ix, 285.

<sup>111</sup> Annals of Surgery, 1920, lxxi, 47.

of the graft being mushroomed through the opening in the bones and then the skin should be closed over the graft with interrupted sutures.

**Osteoperiosteal Grafts.** Instead of the usual graft which includes all layers of the bone tissue periosteum, cortex, medulla, Delangeni<sup>112</sup> removes from the tibia thin layers of bone with their periosteum. The grafts may be taken from any bone provided the two layers of peri-

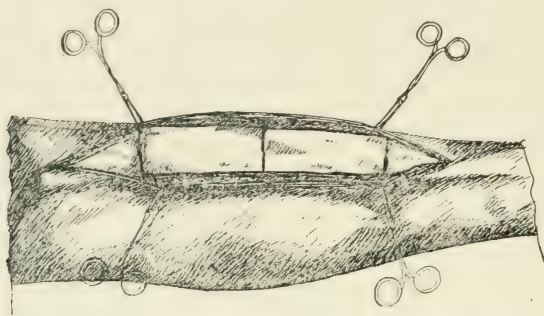


FIG. 81.—The internal surface of the tibia exposed and grafts outlined, one below the other. (Delangeni<sup>112</sup> and Lewin.)

osteum and bone be used, but the internal surface of the tibia is best because of its large size and because it is easily obtained. (If a large amount of bone is to be replaced, both tibiae may be used). The periosteum of the tibia is particularly vascular, and therefore well adapted for easily grafting and secondary rapid vascularization of the bony layer, so that all elements of the callus are supplied namely, living

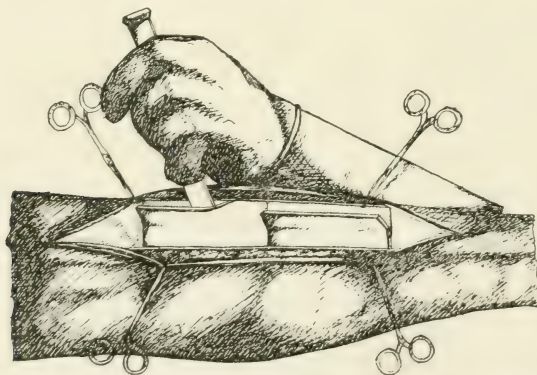


FIG. 82.—Removing the graft by means of the chisel. The graft curls up as it is being removed. (Delangeni<sup>112</sup> and Lewin.)

periosteum and bone, the latter being indispensable in the production of new bone. He does not enter into the discussion of the production of new bone, but says that it is certain that a layer of bone with its periosteum produces new bone and that this bone gradually grows and replaces

<sup>112</sup> Surgery, Gynecology and Obstetrics, May, 1920, No. 5, xxx, 441.

lost bone, and assumes the shape of the bone to be reconstructed. Further, the osteoperiosteal graft need not necessarily be in contact with osseous tissue, but can be kept alive and growing when transplanted into soft tissues. In two of the author's cases, when preparing the bony skeleton of a nose for an Italian graft, the bone was planted beneath the skin of the forearm. The graft is taken from the internal surface of the tibia, using a single bevel engraver's chisel, and a hammer or mallet. A long incision is made through the skin over the middle of the internal surface of the tibia, without cutting the periosteum. The periosteum is then exposed thoroughly and the graft outlined with a scalpel.

The size of the grafts is determined by the defect to be covered. Following the outline, the graft is removed with a chisel. The bevel is kept high and the cutting edge firmly against the bone. By varying the inclination one obtains the proper thickness which is approximately that of a ten cent silver coin. When the graft is removed, it is placed in a gauze compress and immediately transplanted into the wound which is to receive it. The general considerations which apply to all grafts are as follows:

1. Strict asepsis. Slight suppuration will not prevent the graft from taking, but will cause delay. Infection will often cause the elimination of the graft.

2. Antiseptics should not be used because they reduce the vitality of the graft.

3. Bones to be grafted must be entirely free from osteitis. The skin must be healthy and of sufficient amount of elasticity to permit an easy closure of the wound.

4. It is necessary that both surfaces of the graft come in contact with living tissues, so that there will be no dead spaces. The extremities of the graft must be in contact with the ends of the bones to be repaired.

5. The graft should be held in place by means of catgut suture placed through the muscles.

All dead spaces must be obliterated by this means.

**Roentgen-ray Diagnosis of Bone Lesions.** Lovett and Wolbach<sup>113</sup> state that considering the behavior of bone in general, as studied by the  $x$ -ray, it seems to be a structure of very limited reaction to pathological conditions. As shown in the  $x$ -ray, there seems to be three possible reactions in bone. These are: (1) Atrophy or diminution in lime content. (2) Destruction of bone tissue, which may be local or general. (3) The formation of new bone or a condensation of existing bone around a focus of disease. The problem of differentiating tuberculosis, osteomyelitis and syphilis by the  $x$ -ray they feel is very difficult. When the lesion shown is purely a destructive one, it is most often tuberculosis. A lesion of rapid destruction, with marked formative activity is generally osteomyelitis. The purely formative processes are most likely to be syphilis.

In conclusion, they state that the diagnosis of infectious bone lesions would be much simplified if each infectious agent always produced the

<sup>113</sup> Surgery, Gynecology and Obstetrics, August, 1920, No. 2, xxxi, 111.



same reaction. The pyogenic bacteria alone may be counted upon to conform to type; namely, first the destruction of tissue to be followed by repair, which in a case of bone means necrosis with more or less disappearance of lime salts followed by new bone formation from adjacent healthy bone structures. It must be remembered, in the reaction of bone to injury, that new formation of tissue is always by ossification and therefore that granulation tissue from bone or periosteum becomes bone tissue. The above simple sequence in the pyogenic infections account for the definite changes we see in osteomyelitis.

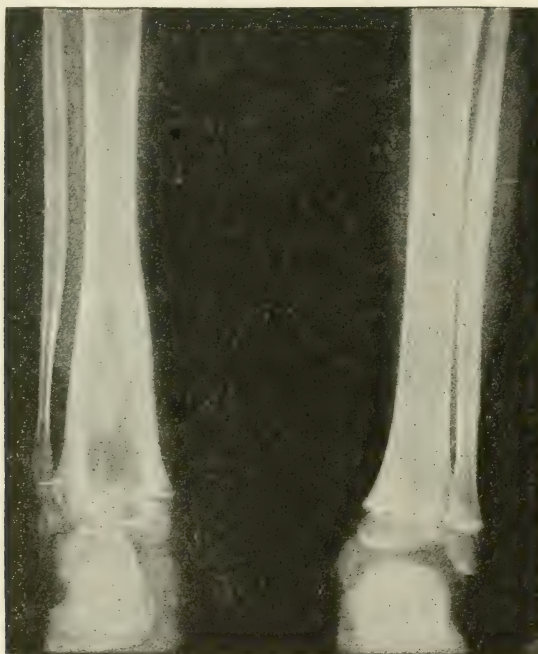


FIG. 83.—Case 1. (Lovett and Wolbach.)

Syphilis affects the bone in two ways: Destruction of the bone or the new formation of bone. Both effects may occur in the same case. Destruction of bone follows the formation of local, rapidly formed gummatous lesions, sometimes of endosteal and periosteal origin, sometimes of perivascular and extending into the bone. On the other hand, the degree of reaction of the spirochæta may be slight and result only in proliferation of cells of the periosteum and endosteum resulting eventually in new deposits of bone.

Tuberculosis presents more possibilities. In soft tissues it is known that the tubercle bacillus can duplicate the reaction of almost any type of pathogenic organism. Thus the various types of exudative response to injury may be the result of the tubercle bacillus alone; fibrinous or purulent exudates are frequently found upon serous membranes which are produced by the tubercle bacillus. In bones we usually think of

tuberculosis as a proliferative process resulting in the new formation of tissue, and this is the most frequent type of tuberculous bone lesions and it gives rise to the formation of bone cavities without a peripheral reaction or condensation of bone.

The important lesson from the pathologic study of this series of cases is that tuberculosis in bone may simulate any other infectious process, both in location and character of the lesion. Frequently, therefore, diagnosis of tuberculosis of the bone cannot be made from x-ray studies alone, and other clinical evidence is necessary. The only certain method is by pathological examination.

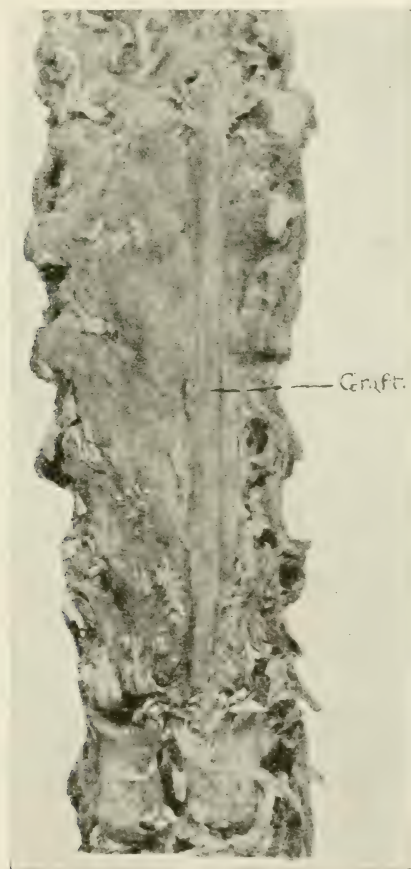


FIG. 84.—Posterior aspect of specimen. (Ely.)

**Ankylosing Operations on the Tuberculous Spine.** Ely<sup>114</sup> reports the postmortem specimen obtained from a boy of four years upon whom he first did a Hibbs operation. Five months later he did a second operation and found that bony union had been attained for the most part, but was

not complete in one or two places. The laminæ were carefully bared and where non-union was suspected, a chip was turned down from the lower border, as in the Hibbs operation. In addition, a piece of the cortex of the tibia was removed and sutured tightly to the laminæ with kangaroo tendon. Three months later death occurred, and the affected portion of the spine was removed. Examination of the posterior portion of this specimen showed a tightly adherent periosteum. When this was

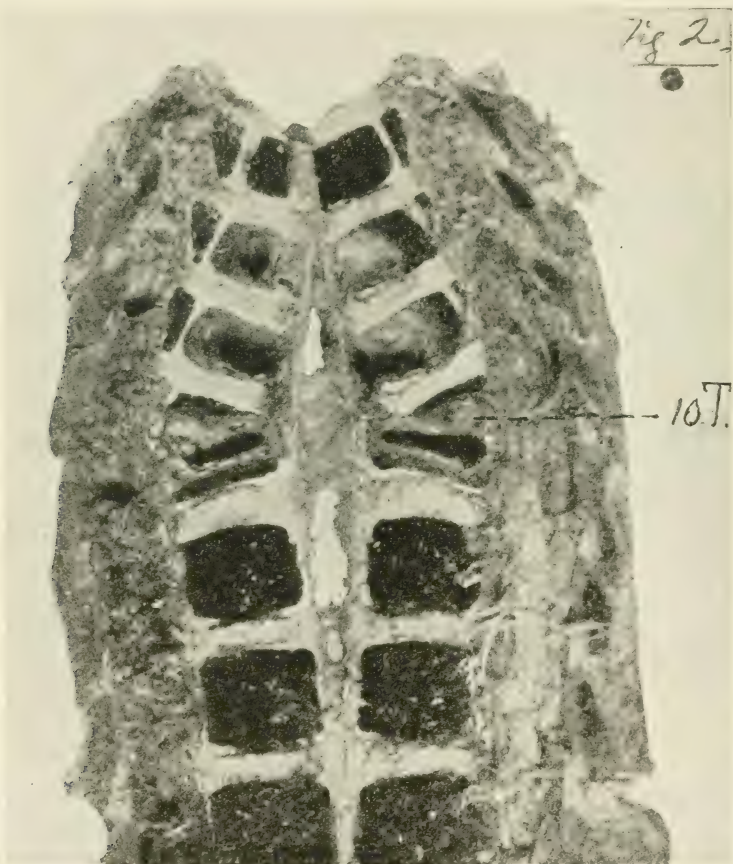


FIG. 85.—Specimen laid open from behind. (Ely.)

dissected off, a solid bridge of bone uniting the eighth, ninth, tenth, eleventh, twelfth thoracic and first lumbar vertebræ was discovered. This bridge of bone seemed to be the result of the union of the laminæ produced by the Hibbs operation, reinforced by the graft, and the graft was apparently firmly united to the lateral masses. The bony structure of the graft was continuous with that of the receiving bone. The specimen was sawed sagittally and split open from behind. There was marked destruction of the eighth, ninth, and tenth vertebræ, but the eighth and



ninth had been kept from collapsing by the bony bridge of laminae. In spite of this bony bridge, the disease had steadily progressed.

He concludes:

1. That ankylosing operations for spinal tuberculosis are curative in a large proportion of cases of what was previously an almost incurable disease.

2. They are not invariably curative. Unlike ankylosing operations on other joints of the body they ankylose neighboring joints, and not the diseased ones, and hence simply provide a splint for the affected region. They provide rest, nothing more. They put Nature in the best possible position for accomplishing a cure herself, but they cause no change in the effected tissues. The lymphoid marrow and the synovial membrane still exist, and afford the proper food for the tubercle bacillus. Consequently, we occasionally observe a steady progress of the disease, and must do another operation above or below the first one, when the tubercle bacilli invade the bone narrow above or below the ankylosed area.

3. These operations shorten greatly the length of the treatment and make it much simpler. Complications, such as abscess formations and paraplegia, usually are not found to follow them. Apparently they often cure paraplegia.

4. They are serious operations. At least 11 deaths have been recorded in literature. Death is sometimes caused by the anesthetic, hence they should never be done without a skilled anesthetist. The patient should always be anesthetized in a prone position with an arrangement of cushions under his shoulders and hips that will enable him to breathe comfortably.

5. Opinions differ as to the relative merit of the two operations. Ely prefers the Hibbs operations, but confesses it is more difficult, and he never undertakes it in a lordotic lumbar spine. The Hibbs operation requires almost two hours, while the Albee operation should take about forty-five minutes.

**Injuries of the Semilunar Cartilages of the Knee-joint.** Henderson<sup>115</sup> points out that the semilunar cartilages are fibrocartilaginous structures placed within the knee-joint to deepen the cavity for the reception of the condyles of the femur. They are wedge-shape, with their apices to the center and their bases to the periphery of the joint. Their presence allows a more even distribution of the wear and tear on the joint surfaces than otherwise would occur. The external cartilage is less intimately associated with the capsule of the joint, and being more free it can readily slip from the grasp of the external condyle and the external tuberosity of the tibia. It is thicker, broader, and more nearly circular than the internal cartilage, and on this account we find the area of contact between the external condyle of the femur and the external tuberosity of the tibia less extensive than the contact on the inner side of the joint. We have in the past erroneously spoken of a loose semilunar cartilage as being the cause of mechanical derangements of the knee-joint. While it is possible that an internal semilunar may be abnormally mobile, the vast majority of so-called derangements are in reality fractured or torn semilunar cartilages.

The history of these semilunar injuries is usually very definite. The patient is most frequently a male, under thirty-five, in the active period of life. The accident occurs while exerting some muscular movements, as in games or running, and with the knee in moderate flexion and the foot or leg in external rotation. When extension is attempted, in such a situation, the internal condyle of the femur catches the cartilage and one of three things must take place to avert disaster: The force must be stopped; the cartilage must slip out of the grasp; or the cartilage must be firm enough to stand the pinching, crunching force inflicted on it. It is usually impossible to stop the contraction of so powerful a muscle as the quadriceps in time to prevent injury. The cartilage usually is not able to stand such extreme force and rips or tears in its longitudinal axis: the

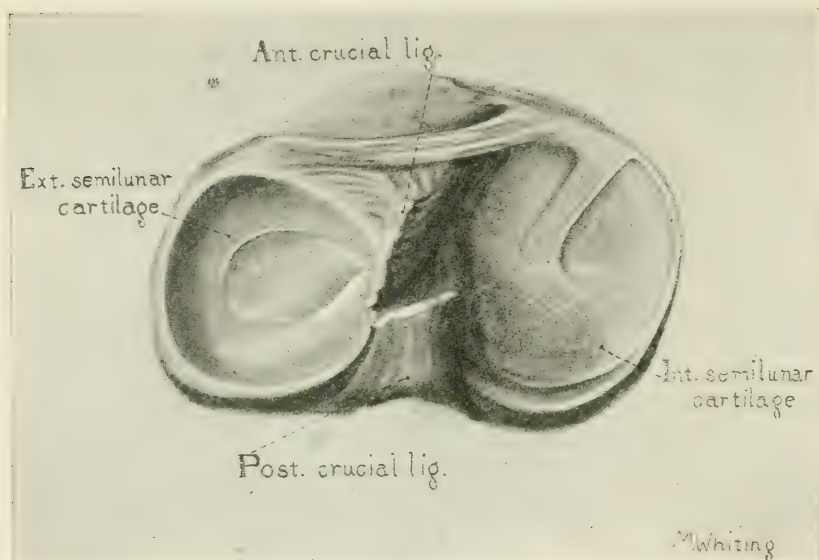


FIG. 86.—Internal semilunar cartilage displaced to the mesial portion of the joint; anterior portion blocking extension; called bucket-handled type by Rutherford Morison. (Henderson.)

condyle of the femur forces the detached portion to the mesial portion of the joint, and thus prevents extension, the knee being locked in partial flexion. The subjective symptoms are severe pain and immediate disability. The pain is not due to the tear in the cartilage, since the semilunar cartilages are not supplied with nerves, but to the stretch of the ligaments, which is also, of course, the cause of the complete disability. Most of the pain is referred to the inner side of the knee just anterior to the internal lateral ligament and, if there is not much synovial effusion, a small protuberance may be felt in this region. If the semilunar cartilage is torn, it is best to immediately reduce it. A recurrence of the locking depends upon the promptness with which reduction is obtained and whether or not the part is kept at rest long enough to permit of healing.

By far the most common tear is the so-called "Bucket Handle" tear of Morison. It consists of a displacement inward of the torn middle three-fifths of the meniscus, so that it lies mesially to the internal condyle. It is attached to the anterior one-fifth and to the posterior one-fifth, so that it blocks complete extension. In chronic recurring cases, it is surprising how this condition can exist and the patient still be active and able to get about with only a slight disability of incomplete extension. There are other types of tears but, in Henderson's experience, this

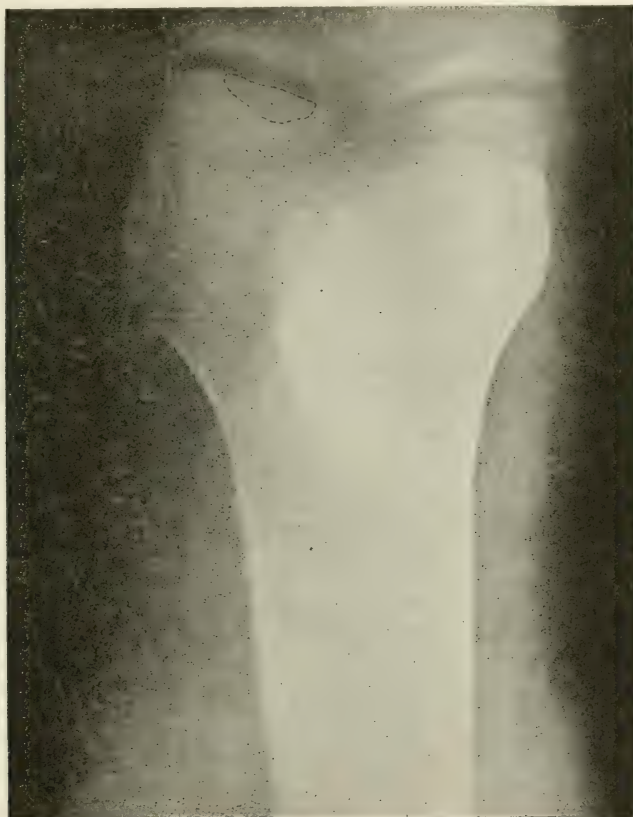


FIG. 87.—Osteochondritis desiccans. Loose osteocartilaginous body lying at the site of origin. (Henderson.)

is the most common. The early attacks are usually accompanied by swelling and pain, but as they become more frequent the symptoms become less marked as a tolerance becomes established. There is no periarticular thickening if the injury is due solely to a lesion of the semilunar, and one should be very slow to make a diagnosis of this condition in the presence of thickening. Periarticular thickening always means arthritis. Again, the presence of any residual symptoms between the attacks are rare and almost exclude injury to the semilunar cartilage.

In making the differential diagnosis, tuberculosis of the knee, particu-



larly of the synovial type, with its mild symptoms, is often confusing. Fringes of the thickened synovia being nipped between the joint surfaces, give pain simulating locking of the joint, but the chronicity and the periarticular thickening, persistent effusion, and absence of severe locking should differentiate it. The chief condition to be differentiated is osteochondritis dessicans. Hypertrophic arthritis or osteochondromatosis, the loose body may be felt, but, unlike the semilunar cartilage, it varies in its position and may be felt above the patella and to the outer and inner side of the joint. In osteochondromatosis the bodies are usually numerous and are easily felt at all times. The x-ray will usually show these foreign bodies while it will rarely show any changes when the semilunar cartilage is damaged.

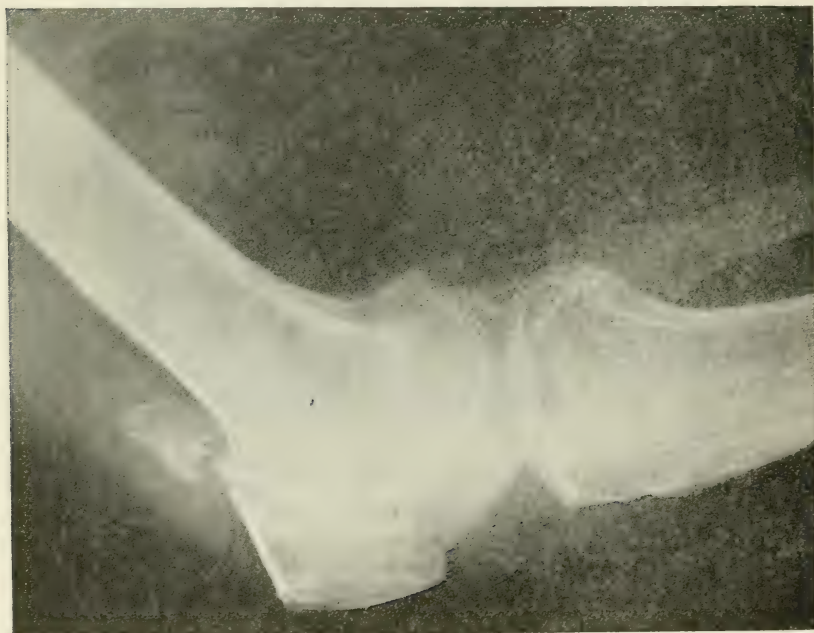


FIG. 88.—Osteocartilaginous loose bodies due to hypertrophic arthritis.  
(Henderson.)

*Treatment.* The surgeon should attempt to immediately reduce the torn or fractured cartilage. It is rarely necessary to give an anesthetic. The patient is placed on his back upon the floor, the knee flexed to the limit, the thigh to well beyond a right angle, and, suddenly, when the patient is off guard, with the thumb pressing over the anterior attachment of the cartilage, the knee is extended. The patient should be able to tell you whether it has been reduced, and his opinion should not be disregarded. If the reduction is complete, as indicated by complete extension of the joint, together with the statement of the patient, the leg should then be put in a plaster cast for four weeks. This may insure such healing that recurrence will not develop. When there is

no question that reduction can be accomplished by conservative measures, the joint should be opened. This means after more than one locking of the joint has occurred. Jones and Lane feel that recurring locking of the joint may be the cause of the development of tuberculosis in such a knee. The recent war has definitely shown that the knee-joint has a considerable resistance to infection and if the degree of asepsis is used, as in the abdomen, no fear need be entertained regarding exploration of the joint. Benzine and iodine preparation is sufficient.



FIG. 89.—Osteocartilaginous loose bodies due to osteochondromatosis. (Henderson.)

*Operation.* After the patient has been anesthetized, he is placed in a slight Trendelenburg position and the foot of the table is dropped so that the knee is on an angle of 140 degrees flexion. The triangular space bounded by the patella and patella ligament, the head of the tibia and the internal condyle of the femur is readily outlined and may be opened by a curved or straight incision. If there is no fracture or tear in the cartilage, the surgeon should hesitate about removing the meniscus. A pathologic condition should be evident before any structures are removed. If exposure of the cartilage is difficult, the incision in the capsule may be

enlarged, but care should be taken not to injure the internal lateral ligament. Outward rotation of the foot and leg, with the knee still in

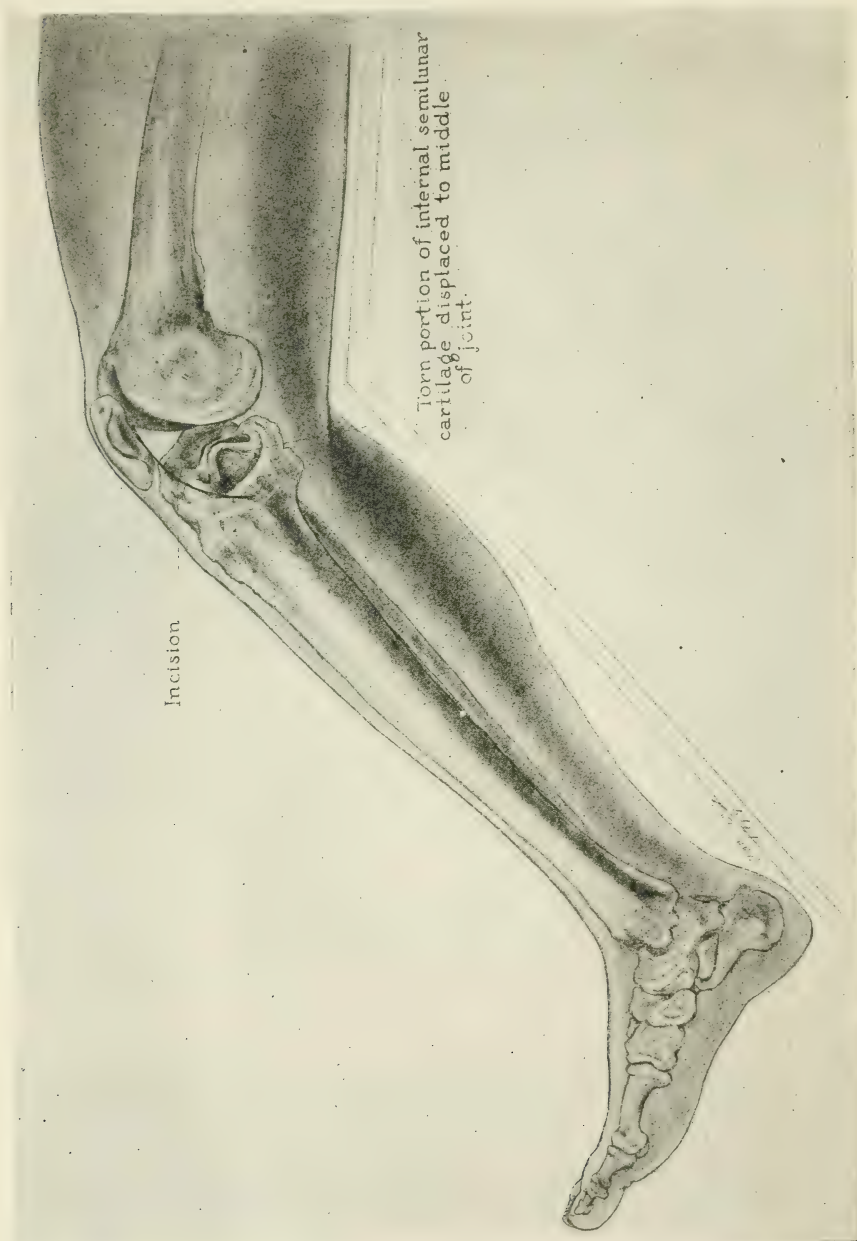


FIG. 90.—Incision used with leg flexed at an angle of 140 degrees. (Henderson.)

a semi-flexed position, will also give a better exposure. It is generally sufficient to remove a little more than the anterior three-fifths of the



thus avoid injuring the ligament. The capsule should be closed in layers, using plain catgut. A plaster-of-Paris cast from the groin to the ankle is applied, with the knee in extension, and may be removed on the eighth day. Function is permitted as soon as the patient desires it.

**Treatment of War Wounds of the Joints.** Though the early closure of wounds of the knee-joint was first done in 1915 by Delorme, of Lyon; by 1916, during the battle of the Somme, this practice became the rule. Duval<sup>116</sup> outlines the following principles upon which immediate suture is based. A war wound, a joint, like any other wound, is contaminated directly by germs which are carried into the wound by the missile and fragments of clothing. The same rules apply here, in development of infection, as have become recognized in the infection of all traumatic wounds through the work of Carrel and Dakin, but the defensive action of the synovial membrane, curiously contrary to our previous teaching, seems to possess a higher bactericidal power than any other tissue of the body. This work was reviewed in *PROGRESSIVE MEDICINE* last year, but the cases reported in the following illustrations by the master of this newer surgery are worthy of reproduction.

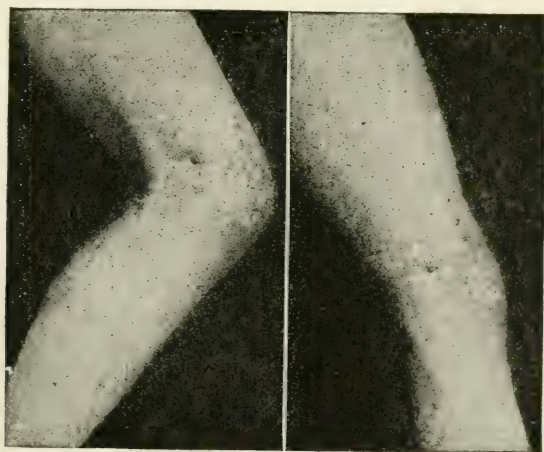


FIG. 91.—Result forty-two days after suture wound of the calf and knee (1918). The shot entered the calf and lodged in the condyle. Primary suture of the knee and secondary suture of the calf. (Duval.)

**The Flail-joint.** Jones<sup>117</sup> states that the flail-joint may follow (a) as a direct result of excision; (b) removal by the surgeon of large comminuted pieces of bone; (c) the direct loss of bone from the foreign body; (d) the extrusion of necrosed bone during sepsis.

In order to preserve joint function (a) the extent of bone excision should be strictly limited, and only as much taken away as safety demands; (b) the extension that is applied should be very moderate and of short duration; (c) in the after-treatment, ankylosis should be aimed at rather than mobility.

<sup>116</sup> *Surgery, Gynecology and Obstetrics*, September, 1919, No. 3, xxix, 222.

<sup>117</sup> *Ibid.*, January, 1920, No. 1, xxx, 6.

(a) *The Limitation of the Extent of Excision.* It is very important that muscular attachments which have important influence in maintaining good function should be spared when possible. The tuberosities of the humerus; the nerve supply of the deltoid; the condylar attachments

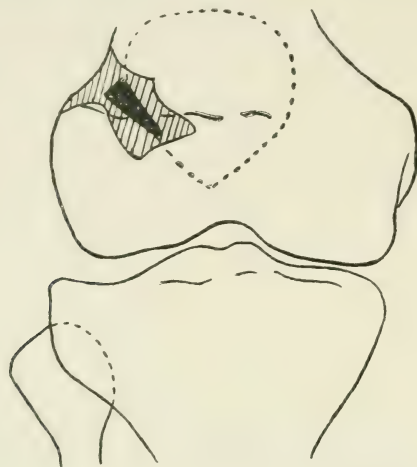


FIG. 92.—Schematic drawing, showing destruction of bone. (Duval.)

of the muscles governing the elbow; the triceps expansion; the biceps insertion; the coronoid and, if possible, the whole or a portion of the olecranon should be preserved. One should endeavor to retain as much as possible of the width of the lower end of the humerus. If it is impossible to leave the important muscular attachments *in situ*, it may be

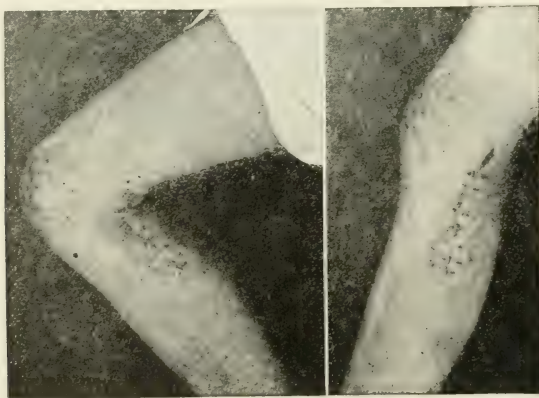


FIG. 93.—Result twenty-eight days after suture in gunshot wound of knee. (Duval.)

possible to chisel off the portions of bone to which the muscle are inserted, for they may all be useful later for reconstructive purposes.

(b) Extension should be limited both in extent and time. He reports having seen several cases where this was not done and where excision of

an elbow, and the application of a Thomas arm splint for several months, resulted in a separation of many inches of the joint surfaces. Those who have seen the American wounded return from abroad have probably



FIG. 94.—Schematic drawing, showing destruction of bone. (Duval.)



FIG. 95.—Result twenty-five days after suture of the extensor tendons in severe wounds of the astragalus (1918). (Duval.)



all had a similar experience. The extension should be strictly limited to the urgent need of drainage. Strong extension of a limb where the



FIG. 96.—Schematic drawing showing destruction of bone. (Duval.)

joint has been excised obstructs free drainage. The extension, if at all necessary, should be of the lightest kind and maintained for the shortest

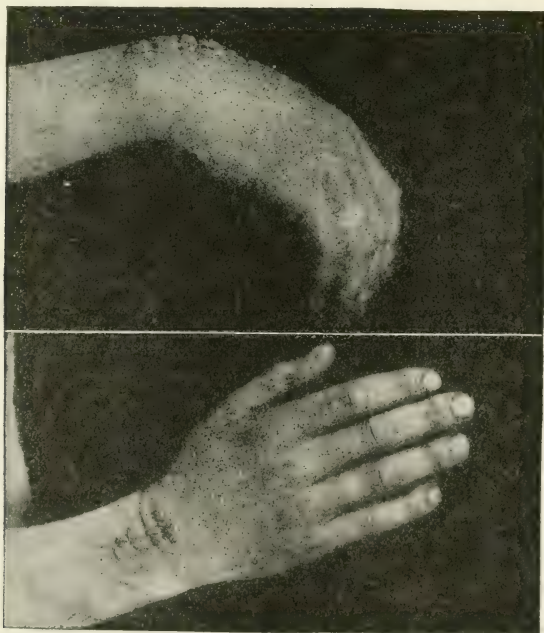


FIG. 97.—Wound of the wrist by fragment of shell. Result after ten days. (Duval.)

period possible. An abducted shoulder and a flexed elbow admit of excellent drainage. In the case of the shoulder and the elbow, the

dependent position of the arm and forearm permits of purulent tracking down the muscular planes.

(c) The aim should be for ankylosis in the best functional position. One rarely attains it, but the effort results in the best possible conditions for future reconstruction. The surgeon, therefore, should, as soon as he can do so, place the bones as near together as possible and in the best position for future function whether pseudo-arthritis or ankylosis occurs.

**TREATMENT OF THE FLAIL-JOINT.** The flail-joint, as we see it, is practically useless from the point of function. The treatment may consist of (a) removal of necrotic bone and scar tissue; (b) correct posture; (c) operative attempts at improved pseudo-arthritis; (d) production of ankylosis; (e) retention in mechanical apparatus.

(a) A fair proportion of flail-joints are complicated by infected bone with discharging sinuses. These should be treated like osteomyelitis elsewhere, *i. e.*, by excision of sinuses, scars and infected bones and the

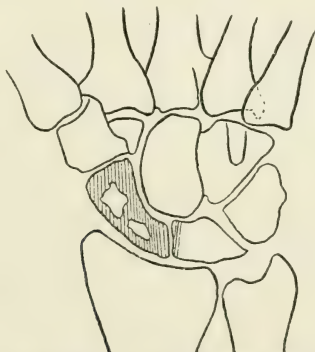


FIG. 98.—Schematic drawing, showing destruction of bone. (Duval.)

resulting cavity chemically sterilized. A surprising proportion of cases, following this, ankylose or result in a much firmer pseudo-arthritis. The shoulder and elbow are joints most responsive to this treatment.

(b) *Correct Posture.* The shoulder should be placed in the functional position by means of an abduction splint. The bones should be opposed without crumpling the soft tissue between them. The fixation should be maintained for at least three months.

(c) Attempts may be made toward improving the stability or retaining the mobility of a weak pseudo-arthritis by operation. This latter should only be attempted when the muscles governing the joint may be reasonably expected to recover strength.

(d) *Ankylosis of the Flail-joint.* In the *hip*, if the femur has lost only the head and the neck, all that is needed is to correct any deformity which obstructs walking, such as abduction. This can be done by division of the adductors. If the limb cannot bear weight, a jointed caliper, that is, a caliper allowing flexion at the knee, should be applied. This supplies an artificial lever, and the muscles governing flexion are enabled to resume their function. With such a splint, the patient can

walk long distances with ease and comfort. The same splint can also be used when the trochanter and part of the shaft is lost. Bone grafting has a very limited application in the upper part of the femur. Ankylosis of the hip is of no advantage and certainly does not justify the severe operation which it would necessarily entail. Mechanical measures should be adopted in place of operation whenever possible.

*Knee-joint.* Ankylosis of the knee-joint is the only practical treatment for a flail condition. The sawing of the ends of the bone and the fixing of them with a screw or nail is all that is required. If there is a wide separation, it may be necessary, after sawing the ends of the bone, to bring a bulky, sliding graft from the tibia or femur; and wedge it in a groove at right angles to the line of the joint. If there is shortening of many inches, the patient may prefer an artificial limb, and his arguments may be worthy of the physician's consideration. If an operation is refused, the caliper splint and a high boot will afford the best help.

*Ankle-joint.* A flail ankle is so rare that Jones cannot recall an instance as result of a war wound. Should it be met with, the treatment will lie between an ankylosis or amputation.

*Shoulder-joint.* He prefers the production of ankylosis by end-to-end apposition. The joint should be fully exposed and the glenoid gouged as deeply as possible. The base of the coracoid and the acromion should be chiseled and the bony flaps left. The upper part of the humerus is then exposed and sawed through, and a groove made into the upper part of the shaft for the reception of acromion. The humerus is pushed into the glenoid and the partially sawed acromion pressed into the groove especially prepared for it. The glenoid, humerus and acromion should be fixed in contact by kangaroo tendon and the arm placed in the functional position. If there is no loss of bone, this position is just in front of the coronal plane of the body, while if there is much loss of bone, it should be fixed in the plane slightly posterior to this. Before an arm is ankylosed, care should be taken to ascertain whether the scapula is mobile. Also, whether it retains its normal position in regard to the humerus. This is extremely important. The success of the operation depends on sound ankylosis and a mobile scapula. If the scapula is fixed and the arm abducted, the result of the operation is a tragedy, for the patient will have a fixed abducted shoulder with an arm he cannot lower. After operation, the scapular muscles should be reëducated by exercise.

*Elbow-joint.* Two methods of treatment are advocated for flail elbow. (a) The non-operative, (b) the operative. (a) The non-operative method consists of the approximation of the bone ends, counteracting the effect of gravity, and in muscle reëducation and development. It also often involves the wearing of apparatus. (b) The operative treatment has one of two objects (1) the formation of bony ankylosis, (2) the provision of a mobile arm with stability. The non-operative treatment is only likely to be successful where there are broad ends to the bone. This also applies to the operative treatment. From the nature of the bone ends no one routine operation can be prescribed. The underlying principles, however, are the freshening of the bone ends, the



splinting of them without detaching the fragments and enlarging the area of bone apposition as much as is practical, and then firmly immobilizing.

**Focal Infections.** Alvarez<sup>118</sup> makes a timely protest against the reckless extraction of teeth. One of the saddest features in this indiscriminate pulling of teeth is that, in many of the cases, an experienced physician should have been able to have foretold the unsatisfactory outcome and to have warned the dentist to proceed cautiously and conservatively. The arthritis may have plainly been gouty or tuberculous, or the pains in the shoulders may have been due to degenerative changes in the aortic arch, and in some instances it is quite obvious that the physicians may have ordered the extraction of teeth simply because they believe or hope it is a panacea for all diseases. "He believes that we have lost our heads over this thing and the time has come to call a halt." Startling results have been obtained in some cases by the extraction of teeth but this is no excuse to pull the teeth first, and if the patient returns unbenefited to hunt further to discover what is the matter with them. "In the middle ages if a man died it was because he had not been bled enough, or because it had not been done from the right vein." Today we know that bleeding is useful in only a few conditions. Similarly, the day will come when focal infections will not be dragged in to explain all ills of the flesh. Let us by all means continue to look for alveolar abscesses, but, if we are to keep the respect and confidence of the public, if we are to avoid damage suits, we must be more careful of our promises to our patients in return for a toothless mouth. Before deciding whether any or all of the suspicious teeth are to come out, the physician must carefully examine the patient. If he is young and sound, and if he has a dangerous arthritis, endocarditis or severe headache for which no other cause can be found, we are justified in insisting on thorough removal of diseased tissues, but when the patient is old and failing, with high blood-pressure, arteriosclerosis and nephritis, we should be careful and consider all the factors involved. If the infected teeth are not serviceable, if they are loosened, perhaps hanging to wobbly bridges, or if their crowns are gone, there need be no question as to their removal, but otherwise let us be frank with him and tell him that their removal will be more or less of an experiment and if he wants to leave no stone unturned in his treatment, he can try it.

We must be careful also in our promises to those patients who, in addition to their root abscesses, have other sources of infection which cannot be so easily removed. Chronic bronchitis, sinusitis, prostatitis and urinary infection, while pelvic inflammation and gall-bladder disease must also be considered.

Alvarez believes that the main reason for our disappointments in the results following the extraction of teeth is that, in many, the alveolar abscess have no demonstrable influence on the patient's health. Time and again one sees powerful and healthy men with large alveolar abscesses

<sup>118</sup> Journal of the American Medical Association, October 18, 1919, p. 1179.

which they have carried for the most of their lives and without a symptom. When further bacteriologic work has been done, we may find that some of these abscesses are sterile, the bacteria having died out just as they do in pus tubes. Again, the necrosis may never have been infectious in origin, but may have been produced by the chemicals used during the preparation of the root canals. Many of the dentists have become so frightened over the terrible results which they think must follow every root infection that they are refusing to fill any root canals at all. Certainly the thousands of people who, for the last thirty or forty years, have been chewing contentedly on dead teeth (without signs of root infection) should be grateful that these radical ideas did not prevail when they were young. The body has wonderful defenses against bacteria. These defenses are particularly efficient in the mouth. Though bacteria are constantly getting through the first line of defense, they are being stopped by the second, and in many cases it is able to protect itself from the activities of a few invaders which have reached the apex of a tooth.

**Chronic Arthritis.** Chapman<sup>119</sup> (1) reports 50 per cent. of the cases of chronic arthritis treated at the Stanford University clinics by the removal of foci of infection (according to clinical observation) showed definite improvement. (2) From his personal observation of 21 cases (a) 76.2 per cent. showed definite improvement; (b) 19 per cent. showed no improvement or change; (c) 4.8 per cent. were worse after the treatment. (3) Although the percentage of improvement did not vary greatly in the different groups, the most striking results were obtained in those cases in which the focus was situated in the genito-urinary tract. (4) Long-continued, faithful treatment is necessary before improvement can be expected in the cases in which the focus is located in the genito-urinary tract. (5) Very rapid recovery with very few treatments was obtained in those cases in which the teeth was the seat of infection. (6) Removal of the tonsils in several cases was followed in a few days by loss of pain, and later by return of function to the injured joint.

**Osteochondritis Deformans of the Hip-joint in the Young.** Sundt<sup>120</sup> ascribes the priority in a description of this obscure infection of the hip-joint to Waldenstrom, Calve-Legg-Perthes. They all, except Perthes, protest against the term osteochondritis as it is not an inflammatory lesion. The special characteristic is the flattening of the head, as weight-bearing crushes it flatter, when nutritional disturbance has interfered with its proper development. Waldenstrom proposes that the term coxa plana be given, in contradistinction to coxa vara and coxa valga. It could be supplemented by the descriptive terms, traumatic, tuberculous, etc. Perthes, on the other hand, insists upon the name osteochondritis deformans juvenilis, as this classes it with the osteochondritis desiccans of the knee-joint, for both of them are a result of nutritional

<sup>119</sup> *Annals of Surgery*, May, 1920, No. 5, lxxi, 652.

<sup>120</sup> *Zentralbl. f. Chir.*, Leipzig, May 29, 1920, No. 22, vol. xlvii.

disturbance from impeded circulation from some cause. Perthes cites a number of instances of bilateral development, which suggests that a more general disturbance than trauma may be involved in its etiology. Legg calls the condition osteochondral trophopathy of the hip-joint.

**Benign Exostoses.** Eliot<sup>121</sup> says that nutritive disturbances and trauma have long been recognized as important factors in the causation of exostoses. Those arising from nutritive disturbances spring from the epiphyses that are concerned in the growth of the bone, they are occasionally multiple and frequently disappear when the nutritive disturbance is corrected. Exostoses resulting from trauma most frequently follow prolonged irritation, as the friction caused by horse-back riding, at or near the inner surface of the lower epiphysis of the femur. The effect of acute trauma acting at a distance from the epiphysial line, and at a time when the full growth of the bone has been attained, is reviewed in this article by Eliot. Contusion of bone, like that of the overlying soft parts, causes a variable rupture of bloodvessels with extravasation of blood in the direction of least resistance. If the periosteum is unbroken, this blood collects beneath it, usually in such small quantities as to cause no perceptible swelling. As in the soft parts, the clot usually is absorbed, although more slowly, and at times not without slight permanent irregularities in the contour of the bone due to the calcification of its unabsorbed portion. Rarely, however, as in the case which he reports, the blood is not absorbed, and if it does not suppurate, its persistence, together with its gradual calcification, may cause such a degree of discomfort that the patient is compelled to seek relief. In the absence of suppuration a permanent thickening of the bone, corresponding to the extent of the hematoma, may be ultimately expected, only differing in degree from what ordinarily takes place in the mild type of this lesion. These bone irregularities cannot be classified with the pointed exostoses, but it is possible that subperiosteal hematoma may prove the starting-point of actively growing pointed exostoses which resemble those resulting from continued friction. Though the growth of these benign exostoses is usually slow, they may increase very rapidly in size, as the one reported by Eliot of two inches within thirteen months, and hence raise the question of their malignancy. Microscopical examination demonstrated the benign character of Eliot's tumor.

**Recurrent Intramedullary Osteochondroma of the Femur.** Stetton<sup>122</sup> reported a case of recurrent intramedullary osteochondroma of the femur which had been under his care for nine and a half years. The tumor, when first seen in 1901, involved the great trochanter, extending down the shaft for about 10 cm. A pathological fracture occurred a few days after this x-ray picture was taken, and at the operation a hard cartilaginous tumor was removed subperiosteally. The cavity was curetted and the wound packed open. The section of the tumor showed a hard, homogeneous surface, and microscopically it was composed of small irregularly-disposed spindle-cells imbedded in a hyaline substance. This was apparently undifferentiated osteoid or chondroid

<sup>121</sup> *Annals of Surgery*, August, 1920, No. 2, lxxii, 228.

<sup>122</sup> *Ibid.*, February, 1920, No. 2, lxxi, 200.



tissue scattered throughout the growth or islands of true cartilage. In places, these cartilaginous islands were undergoing ossification. Apparently perfect union and complete restoration of the bone followed this first operation, but six years later a definite recurrence was shown by x-ray and at the second operation the removal of the tumor tissue left a greater defect than before, and the microscopical examination of the tumor tissue was practically the same as the primary growth, except that in places spicules of true bone appeared. Again the defect filled in. One year later he fell and again fractured the neck of the femur in this tumor area. Another fracture occurred through the shaft in 1918, but up to the present time there has apparently been no recurrence of the tumor.

He refers to Bloodgood's<sup>123</sup> report of an analogous case of LeConte's. This case of LeConte's unfortunately has not been fully reported but will be during this coming winter. The microscopical appearance of the tumor was very similar to that described by Stetten. There were three distinct recurrences which involved the entire medullary cavity, then a fracture of the middle of the shaft and an extensive recurrence which necessitated a hip-joint amputation; and after a period of two years he died of a hemorrhage from the external iliac vessels which involved in metastastic growths in the iliac glands. Unfortunately, this tumor had been considered benign by Bloodgood and other pathologists, and it was upon their advice that the conservative measures only were attempted during the first year.

**Sarcoma of the Long Bones.** Coley<sup>124</sup> reports his experience to date, in the conservative treatment of sarcoma of the long bones, and feels that his observations during the last five years confirm his previous report in which he strongly advocated the conservative treatment of this type of tumor. He feels that it is necessary to present this further evidence because the majority of surgeons at the present time, including many men with wide surgical experience, have not fully accepted the principles of conservative treatment, and are still sacrificing many limbs which might be saved. He now has 250 cases that have come under his observation.

In the question of DIAGNOSIS he emphasizes the following points:

1. *The Element of Pain.* Pain, especially of the deep boring character steadily increasing in severity, is often one of the earliest and most important signs of sarcoma of the long bones. Rheumatism is usually the first diagnosis. Persistent pain is present for weeks or months before there is a probable tumor, or the x-ray discloses any evidence of a new growth. Pain is a more important symptom in periosteal growths than in the central tumors, in fact, central tumors often attain considerable size with little or no pain. He advocates an exploratory operation in cases where there is any reasonable doubt of the diagnosis. If the tumor is a periosteal sarcoma, it is essential to make the earliest possible diagnosis, while on the other hand, it would not be justifiable to sacrifice the limb without a positive diagnosis, nor would it be justifiable to

<sup>123</sup> *Annals of Surgery*, August, 1910.

<sup>124</sup> *Ibid.*, December, 1919, No. 6, vol. lxx.

subject the patient to the discomforts of prolonged toxin or radium treatment, if the condition was a periosteal sarcoma. The danger of metastases resulting from such exploratory operations is, he believes extremely slight, while the advantage of knowing exactly the type of tumor one is dealing with far outweighs the risk.

**GIANT-CELLED SARCOMA OR GIANT-CELLED TUMORS.** Great confusion has long existed regarding the malignancy of the so-called giant-celled sarcoma of the long bones. Bloodgood has reported 47 cases of benign giant-celled tumors in which the ordinary features of malignancy

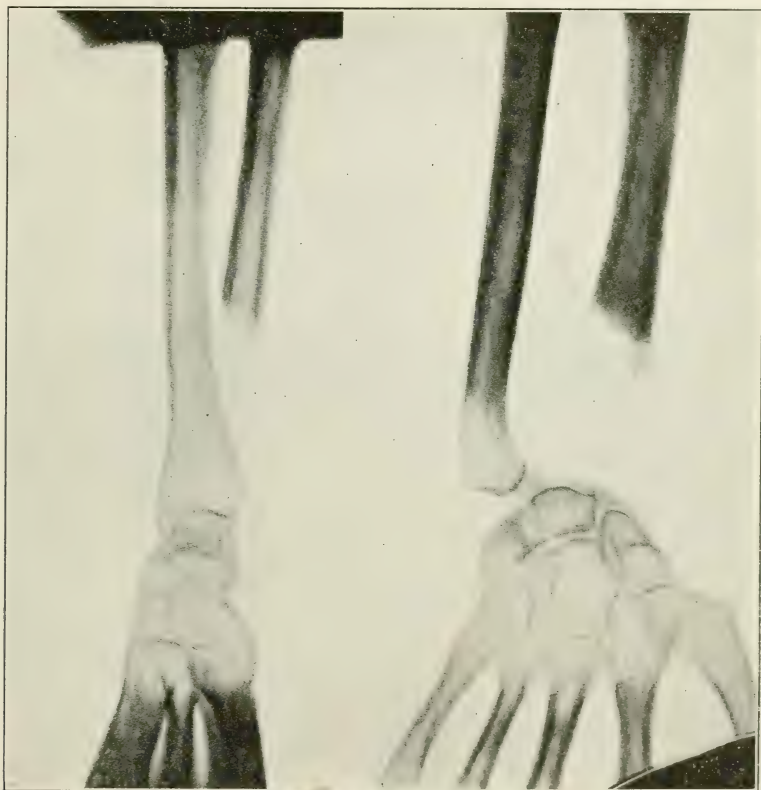


FIG. 99 (Case VI).—Sarcoma of radius before treatment. Cured by toxins alone. Patient well October 25, 1919. Toxins injected into buttocks systematically one year and four months. No other treatment. (Coley.)

were absent. This was reviewed in last year's *PROGRESSIVE MEDICINE*, December, 1919. Coley feels that his experience justifies him in going even further than Bloodgood, urging the employment of conservative methods not only in benign giant-celled tumors, osteitis fibrosa and the like, but actual sarcomas of the long bones, both of central and periosteal origin.

Platou,<sup>125</sup> of Christiana, takes the position that so-called giant-celled

sarcoma is not a malignant tumor at all, but should be classed as a "giant-celled tumor." Though he describes microscopical differences between giant-celled tumors and sarcomas, he concludes that "it is deplorable that microscopical examination sometimes permits only a probable diagnosis. The interpretation of the specimen in question will always depend on a personal opinion. There has not as yet been discovered any test whereby the diagnosis may be absolutely certain either way when the cases are doubtful. The operator, therefore, must take upon himself the responsibility of deciding whether to take the

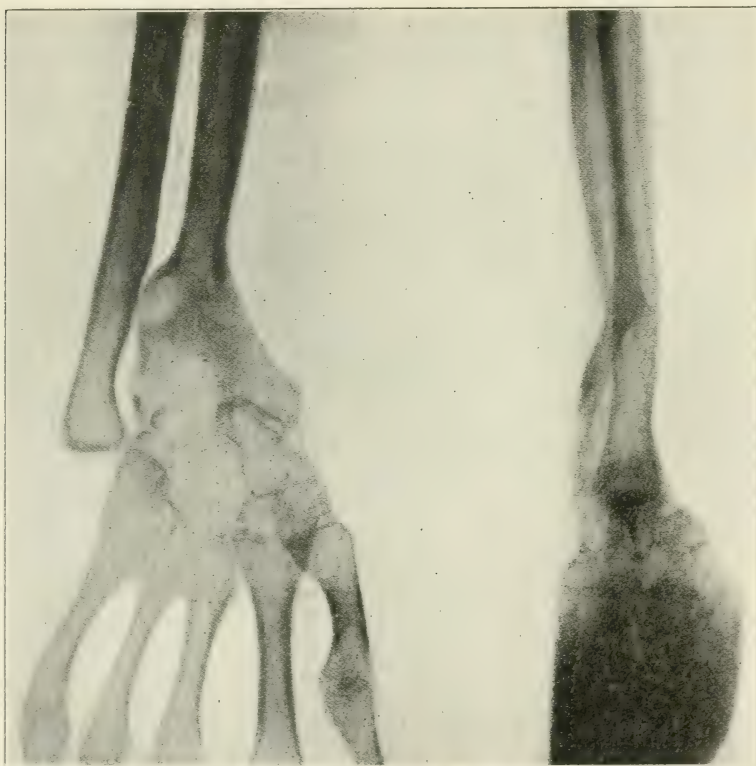


FIG. 100.—Same case as Fig. 99, seven months after treatment. Splint removed, and patient returned to work. Perfect function. (Coley.)

usual course demanded by a diagnosis of sarcoma, or whether the clinical facts of the case justify conservative treatment. If we could always be sure that we were dealing with a benign giant-celled tumor of the long bone, such as Bloodgood described, simple curetting, which he advocates, or, in more advanced cases, resection, would suffice. It is, however, difficult in many instances to determine the malignancy of such tumors.

In Coley's 40 cases of giant-celled sarcoma of the long bone, the diagnosis being made by a number of leading pathologists, 8 of them died of metastases, proving that in certain cases, at least, the tumor



was of a very different type than that described by Bloodgood and Platou.

Barrie<sup>126</sup> feels that the presence of giant-celled sarcomas or giant-celled tumors is certainly no criteria either of neoplasia or malignancy. He regards the bone changes which have been characterized as cystic osteitis fibrosa, bone cyst, and giant-celled sarcoma to be different phases only of a process of attempted repair following bone destruction. The initial cause of this destruction, in solitary lesions, is often trauma, but in multiple lesions the etiology is still a subject for further investigation and study. He feels that the lesions described as giant-celled sarcoma, giant-celled tumor and osteitis fibrosa in bone, present pictures which it is impossible to disassociate from a regenerative process in connective tissue.

The gross and histopathologic study of areas described as sarcomas possess all the essentials of structure of granulation tissue. Further, that the masses of hemorrhagic structure with their giant-celled contents, termed myeloid and giant-celled sarcoma, myeloma and hemorrhagic osteomyelitis, give all the known evidence that we possess of an effort at bone restoration. Exactly the same sort of picture, in both gross and microscopic studies, can be seen in the reaction following fracture of a bone. Thus he would explain these bone lesions as an inflammatory reaction of bone following trauma. First there would be the hemorrhagic structures corresponding to the granulation tissues seen in the repair of all tissues. This, he calls, hemorrhagic osteomyelitis. As this granulation tissue progresses toward the stage of fibrosis and the giant-cell content increases, we have a picture which corresponds to the giant-cell tumor or myeloma. He feels that the presence of these giant-cells are not evidence of malignancy but that here, as elsewhere in the body, they are present as scavengers. In the stage of hemorrhagic osteomyelitis (inflammatory reaction), malignancy is rarely present. As the granulation tissue develops, with the formation of fibrous tissue, we have the condition known as osteitis fibrosa, again rarely malignant. A still further stage in this reparative bone process, would be the bone cysts, also non-malignant. Of course, as in any chronic process, potentialities of malignant growth are present, particularly in such primitive tissue as we have in granulation tissues, and we would expect to find occasionally degenerative malignant proliferative changes, such as Ewing describes under the title "benign giant-celled sarcoma, epulis type."<sup>127</sup> "as the spindle cells of the stroma become more active and abundant, the giant cells diminish, the tumor shows less resemblance to granulation tissue, but becomes firmer and like spindle-cell sarcoma."

It is Barrie's contention then that these bone lesions are really inflammatory reactions, starting first as hemorrhagic granulation tissue and developing into the lesions which have been variously called osteitis fibrosa, bone cysts, medullary sarcoma, giant-celled tumor and giant-cell sarcoma, and further it is his belief that malignant degenerative changes in these processes are exceedingly rare, they should be regarded

<sup>126</sup> *Annals of Surgery*, May, 1920, No. 5, vol. lxxi.

<sup>127</sup> *Neoplastic Diseases*, Saunders, 1919.

as low-grade inflammatory reparative processes and classified accordingly among the regenerative inflammations in bone.

Whether this conception of these bone changes will help us in deciding upon the proper surgical treatment, remains to be seen, at least it sounds reasonable and would make the diagnosis of malignancy in bone changes conform to the characteristics of malignancy in other tissues.

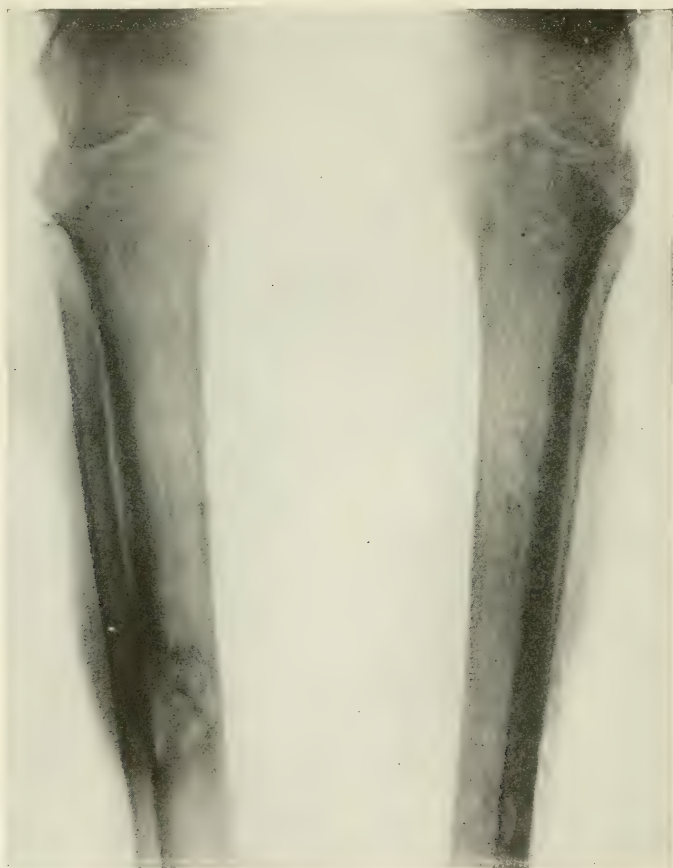


FIG. 101.—X-ray showing large area of osteolysis in left tibia; areas of osteolysis and translucency in right tibia. (Barrie.)

Clinically, Coley feels, in his experience, that myelogenous or mixed giant-celled sarcomas, particularly in the lower end of the femur, are, for the most part, true malignant tumors. In a very small number of cases of periosteal and highly malignant tumors of the long bones, he has been able to save the limb, as well as the life of patients, by the prolonged use of mixed toxins of erysipelas and *Bacillus prodigiosus* and but a larger number of cases of malignant tumors of central origin. If the tumor is certainly benign, curetting alone, as advocated by Bloodgood, is sufficient to effect a cure, but as no one can, at the present time

definitely determine whether these tumors are benign or malignant, it is a risk, to say the least, to limit one's surgical treatment to curetting. True, the location of the tumor gives some indication of the possibilities of malignancy, as a benign tumor in the lower end of the femur, in Coley's experience, is comparatively rare, but, from our present knowledge, it would seem, as suggested by Barrie,<sup>128</sup> "that in addition to curetting all accessible lesions, Coley's toxins and radium should be used in addition."

In dealing with periosteal tumors, we have an entirely different proposition. There is never any doubt about the malignancy of the tumor, all agree that even the most radical operations rarely save the patient's life. Coley advocates an early exploratory operation to definitely establish the diagnosis at the earliest possible moment. The microscopical diagnosis of periosteal sarcoma is, in most instances, much less difficult than in the tumors of central origin. Formerly he advised amputation in these advanced periosteal cases, but since he found that in a number of cases in which the patients absolutely refused amputation he was able to save the lives as well as the limbs of a number of them by the use of mixed toxins, he feels justified in treating even periosteal sarcomas by conservative methods.

The question naturally arises: should the conservative treatment consist in mixed toxins alone or in radium alone, or a combination of both? Experience has shown that toxins, without any other agents, have cured the disease, saved the limb, and the patients have remained well for many years afterward. This is true of every type of sarcoma, both periosteal and central. There is only one case reported in which the patient, after being treated with radium, has remained well as long as five years. This was reported by Pinch of the London Radium Institute, 1918. Coley advocates, in the best interests of patients suffering from sarcoma of the long bones, a combined treatment consisting of the systemic effect obtained by the use of toxins, together with the local action of radium. If the tumor does not show marked improvement in the course of four or five weeks, under this treatment, he advises amputation followed by the use of the toxins as a prophylactic against recurrence. Resection, with or without bone implantation, is, he believes, seldom indicated.

Coley reports the *end-results* of this series of 250 cases of sarcoma of the long bone observed from 1890 to 1919 in the following interesting tables. The serious and almost hopeless prognosis of sarcoma of the long bones from a surgical standpoint was shown at a symposium before the Royal Society of Medicine in London, November, 1912. Of the series of 61 cases observed during the preceeding ten years, all were treated by amputation. Of the 25 cases of periosteal sarcoma of the femur, not a single patient was alive after a three-year period. Of the myeloid type, of 4, only 2 survived the three-year period. Of 8 cases involving the humerus, not a single patient reached the three-year limit. Of 2 radius cases, 1 died and 1 was living after three years.

<sup>128</sup> Annals of Surgery, May, 1920, No. 5, vol. lxxi.



Of 11 periosteal sarcomas of the tibia, but 1 survived for three years, and of 3 of the myeloid type, but 1 was living after three years. Thus, of 61 cases of sarcoma of the long bones, only 5 were living after the three-year period. From St. Thomas's hospital, 28 periosteal cases were reported, and not a single patient living after three years, and 17 myeloid tumors with only 5 living after three years. In contrast, Coley's personal analysis from 1890 to 1919 shows:

Femur . . . . .	117
Humerus . . . . .	54
Tibia . . . . .	40
Fibula . . . . .	8
Radius . . . . .	12
Ulna . . . . .	7
Clavicle . . . . .	11
Metacarpal . . . . .	2
Total . . . . .	251

Of 117 femur cases, 21 were alive and well over three years. Of these, amputation was performed in 15 cases preceded or followed by a course of toxin treatment. In the other 6 cases the limb was saved, as well as the life, by conservative treatment only. Of the 6 cases, treatment only by conservative treatment, 3 were of the periosteal type and 3 central mixed, giant and spindle-cell. Of 53 cases of sarcoma of the humerus, 2 survived the three-year period; in 1 of these toxins alone were used, and in the other toxins first and then amputation after a recurrence six months later.

Of the 40 tibia cases, 8 are known to be well for a period of more than three years. In 4 of them amputation was performed, while in the other 4 the limb was saved.

Of 12 cases of sarcoma of the radius, 4 remained well beyond the three-year period.

In only 1 of them was amputation performed.

Of the 6 ulnar cases, 1 spindle-celled sarcoma, in which amputation was done, remained well for seven years and then died of abdominal metastases. Of the 8 cases of sarcoma of the fibula, not a single patient is known to have survived the three-year period.

Of 11 cases of sarcoma of the clavicle, a total excision was done in 3, followed by the use of the toxins, 2 of them are living after nine years. This group is of particular interest, inasmuch as sarcoma of the clavicle is highly malignant and there are no cases on record, except the Valentine Mott case in which the diagnosis is now believed to be chondroma instead of sarcoma.

In this group of 251 cases, 35 remained well for more than three years. Five of these eventually died from recurrence.

# PRACTICAL THERAPEUTIC REFERENDUM.

By H. R. M. LANDIS, M.D.

**Acacia.** The use of gum acacia in hemorrhage is recommended by Bayliss.<sup>1</sup> He uses a solution of gum of acacia of 6 to 7 per cent. in 0.9 per cent. sodium chloride. This he states is capable of effectively replacing blood lost, unless the loss amounts to more than 75 per cent. of the blood volume. It has no chemical or drug-like action and can be used in large quantities. Its effect is due to the fact that the bloodvessels are impermeable to colloids, so that their osmotic pressure is effective in retaining within the circulation the solution that has been injected, a property which salts do not possess, since the vessels are permeable to them.

This gum-saline solution does not produce anaphylaxis nor hemolysis; nor does it agglutinate the blood corpuscles in man, although it does so *in vitro* in the case of some cats.

The acacia solution is indicated in hemorrhage from various causes, whether from injury, disease or in operations. Bayliss states that it can be used also, with benefit, when the blood volume is reduced owing to a removal of a part from effective circulation by stagnation in the capillaries, as happens in wound shock, traumatic toxemia and probably in other similar conditions. In such cases its primary object is to maintain a normal circulation until the toxic products are eliminated from the blood, while the blood out of circulation is restored to use.

**Acetanilid.** Instances of poisoning from this drug were at one time relatively common. Of recent years addiction to its use seems to be less frequent. Nadler<sup>2</sup> has reported the case of a young woman who began using the drug for the relief of headaches following several operations. She had been taking acetanilid up to 50 grains a day for a period of three years. The usual picture was produced, namely, marked anemia and cyanosis. The urine was reddish brown, as was also the blood-serum. On withdrawal of the drug, the cyanosis and urinary changes promptly disappeared.

**Acetylsalicylic Acid (Aspirin).** In a study of the regulation of this drug in fever cases, Barbour<sup>3</sup> found that in 1-gram doses there is a marked antipyretic effect in febrile, temporarily afebrile and convalescent subjects—while no such action occurs in normal persons. In one and one-half hours the temperature change averaged 0.81° C. on four control days.

The drug also caused an average decrease in the pulse-rate of ten beats per minute. Temporary cardiac disturbances were noted in 2 cases.

<sup>1</sup> Journal of Pharmacology and Experimental Therapeutics, March, 1920.

<sup>2</sup> Journal of the American Medical Association, June 19, 1920.

<sup>3</sup> Archives of Internal Medicine, December, 1919.

The return to the initial temperature level is brought about essentially by a reduction of the heat elimination to about one-half of the normal figure, and is unaccompanied by shivering or marked increase in carbon dioxide output. Barbour states that sensitivity of febrile, temporarily afebrile and convalescent subjects to antipyretics is not yet explained. These drugs do not "stimulate" a "depressed" heat regulating mechanism, nor is sensitivity due to a lack of readily combustible material (dextrose); but the respiratory quotient of antipyretic sensitive individuals appears to be increased by doses of acetylsalicylic acid which do not affect the quotient of normal persons. He believes that further studies of the carbohydrate metabolism may elucidate the question of sensitivity.

Why this drug should provoke increased heat elimination in the presence of fever, but not in health, is not clear. That it is not due to a decrease in the glycogen store of the body as Barbour<sup>4</sup> has demonstrated that feeding a carbohydrate, such as glucose, may actually increase the fall in temperature when acetylsalicylic acid is given, rather than counteract it by increased metabolism.

An instance of *idiosyncrasy to acetylsalicylic acid* is reported by Kitchen.<sup>5</sup> A young man was given 3 doses of the drug at four-hour intervals. The following morning a slight rash was noticed on the face and arms. Although the drug was suspected of causing the rash, another 5-grain dose was given. In two hours there developed a severe form of angioneurotic swelling of the face, especially about the eyes. The entire trunk and limbs were covered with urticaria. The wheals were of irregular shape and varied in size from one-half inch to more than two inches in diameter, and were accompanied by intense itching. The condition, while lasting all of that day, gradually disappeared and by the following morning was entirely gone. The patient, a medical student, consented to take another 5-grain dose in order to see what would happen. In less than an hour the condition described above was reproduced and lasted until the following morning. He was then given 2½ grains, and in less than half an hour the same result occurred and lasted for thirty-six hours. A dose of 1 grain also caused the same phenomena which lasted for about ten hours.

In view of the fact that such small doses later caused the untoward effects, it would seem that the patient had been sensitized at the time the drug was first given.

**Adrenalin.** The effect of *intramuscular injections* of adrenalin (0.5 of a 1 to 1000 solution) has been studied by Wearn and Sturgis<sup>6</sup> in a group of normal soldiers and in a group showing symptoms of the so-called "*irritable heart*." Of 26 normal soldiers, who had gone through fourteen months of severe training, not one gave a positive reaction; that is, there was no increase in the pulse-rate, rise of the blood-pressure or the occurrence of either objective or subjective symptoms. The group comprised of those having "*irritable heart*" numbered 73. Their

<sup>4</sup> Proceedings of the Society of Experimental Biology and Medicine, 1919, xvi, 136.

<sup>5</sup> Journal of the American Medical Association, March 27, 1920.

<sup>6</sup> Archives of Internal Medicine, September, 1919.



symptoms had been of long duration, and, as a rule, antedated their entrance into the army. Of this group, about 60 per cent. gave a reaction which indicated sensitiveness to adrenalin. As adrenalin has a secretive action on the sympathetic autonomic nervous system, it may be assumed that the symptoms and signs induced in the positive cases are the result of a hypersensitive sympathetic nervous system. Wearn and Sturgis were unable to distinguish any clinical differences from an analysis of patients showing positive and negative reactions. Although it was tried to influence the condition, not one of the cases giving a positive reaction was improved, and only 3 giving a negative reaction were able to perform full duty.

O'Hare<sup>7</sup> warns against the use of adrenalin in cases of *hypertension*, as it often causes a terrific rise in blood-pressure and a cerebral hemorrhage may result. In one of his patients a severe attack of angina pectoris followed its use.

In a study of the physiological action of *adrenalin in shock* Erlanger and Gasser<sup>8</sup> reached the following conclusions:

1. The injection of adrenalin for a period of twenty to thirty minutes at such a rate as to maintain a high arterial pressure invariably constricts the arteries of both the somatic and the splanchnic areas. With large doses this constriction may be maximal and outlasts the injection period, it may be, for as long as two hours. This continued constriction is partly due to central action.

2. After sufficiently large doses, the arterial pressure, barring occasional intercurrent phenomena, falls steadily and slowly until the animal dies.

3. The jugular pressure, during or after large injections, shows no constant alteration, at least not of a kind that indicates inefficiency of the heart.

4. The heart may become irregular for a while and occasionally stops suddenly while the arterial pressure still is high.

5. The respiration after large doses often is slowed and may suddenly or gradually fail.

6. The portal pressure is increased, often markedly, during the injection, and may remain high subsequently; but not uncommonly it soon returns to the normal level.

7. The rise in portal pressure undoubtedly is caused by an obstruction in the liver which is so marked as to back up even the small amount of blood that is entering the portal system through the strongly constricted splanchnic arterioles.

8. The circulation may fail suddenly through stoppage of the heart due to direct action of the adrenalin, or to the indirect action of respiratory failure. But more often the failure of the circulation is gradual, the pressure steadily falling until the animal dies. The arterial constriction induced by the adrenalin then lasts until the end. In such instances a reduced blood volume, either real or effective, seems to be the main factor at fault. Apathy, as well as the other signs of shock, are present.

<sup>7</sup> Rhode Island Medical Journal, June, 1920; American Journal of the Medical Sciences, March, 1920.

<sup>8</sup> American Journal of Physiology, August 1, 1919.

9. Evidence is presented indicating that accumulation of blood in the portal area as a result of the increased portal-hepatic resistance is not in itself the cause of the failure of the circulation. For marked obstruction of the hepatic radicles in the liver by the injection of a suspension of lycopodium spores may not lead to the shock-like failure of the circulation that is seen after adrenalin.

10. The failure of the circulation is rather to be attributed to the extreme slowing of the blood-flow throughout the body caused by the constricting action of the adrenalin on the arteries. It is concluded that the cause of the failure is the same as is operative after temporary partial obstruction of the vena cava or of the aorta. This conclusion is justified by the fact that the most striking lesion found in animals dying as a result of any of these three procedures is alike, and consists of tremendous engorgement of the capillaries and venules of the villi of the intestines.

The use of *adrenalin in the treatment of blackwater fever* is recommended by Robertson.<sup>9</sup> He states that this use of adrenalin was first suggested by Barnes, a retired government medical officer of British Guiana. The adrenalin is given in the dose of 20 minims every four hours. After the first three or four doses, the urine clears up remarkably. The action of the adrenalin is not due, in Robertson's opinion, to vasomotor constriction but is to be explained by the balancing of a suprarenal insufficiency, which insufficiency is perhaps the cause of the hemoglobinuria in some cases of malarial infection. No quinine is given. Iron tonics are prescribed during convalescence.

Balfour<sup>10</sup> asserts that injections of adrenalin may be of value in the treatment of *pernicious malaria*, which he states has been shown to be associated with an intense infection of the suprarenals whereby the body is deprived of their normal secretion.

The use of adrenalin (epinephrin) in a case of *abdominal pain* following appendectomy is reported by Van Wavaren.<sup>11</sup> He first gave 50 mg. of dry suprarenal substance daily but later had to reduce the dose to 25 mg. This relieved the pain and the bowels became regular. This dose was then continued on alternate days for two weeks when normal conditions occurred. Later there was a recurrence which was again relieved. A second recurrence was also relieved and after three months there had been no return. He ascribes the benefit of the adrenalin to the fact that it probably stimulates the ganglion cells to better functioning.

During the past four years, Vernet<sup>12</sup> has treated a number of cases of *vertigo* with adrenalin (epinephrin) giving from 5 to 20 drops of the 1 to 1000 solution twice daily for ten days. He then stops and resumes the treatment again. Vernet ascribes the vertigo to a loss of vasotonic balance in the internal ear from disturbance in the sympathetic nervous system. The adrenalin restored the balance by stimulating the nerve

<sup>9</sup> British Medical Journal, August 30, 1919.

<sup>10</sup> Therapeutic Gazette, 1920, p. 473.

<sup>11</sup> Abstract, Journal of the American Medical Association, August 21, 1920, p. 577.

<sup>12</sup> Presse Médicale, July 10, 1920.

terminals, regulating the blood-pressure and by its antitoxic action. Old and advanced lesions of the cochlea were not benefited.

In an experimental study, Lesné<sup>13</sup> found that rabbits can bear twice the fatal dose of adrenalin if it is injected directly into the stomach or small intestine, but, if injected into the rectum, the toxic action seems to approximate that with subcutaneous injection. The liver barrier seems to arrest the adrenalin ingested, while, given by rectum, the wealth of anastomoses of the hemorrhoidal veni allows it to pass directly to the vena cava. For this reason, Lesné advises giving adrenalin by rectum rather than the mouth, as the effect will be much greater and with a smaller dose.

The value of *adrenalin as a means of differential diagnosis* has been investigated by Lowrey and Wright.<sup>14</sup> In 78 psychopathic cases it failed to give results since in some cases of dementia precox there was a rise in the blood-pressure and in others a fall.

**Alcohol.** The merits of prohibition and the propriety of curtailing the use of alcohol as a therapeutic agent continues to be the subject of discussion. Potts<sup>15</sup> protests against allowing hysteria, hypocrisy, and cowardice to influence the settlement of medical questions. It is his belief that the evil effects of alcohol on the human race have been exaggerated and that if alcohol was nearly as potent a factor in causing mental and physical deterioration as is claimed by many, the world by this time should be peopled almost entirely with physical and mental weaklings. He asserts that most of the indictments of alcohol are based on the results of laboratory work and the study of statistics, and that such evidence is often fallacious and not consistent with actual experience.

His conception of the question is summarized as follows: That alcohol is not necessarily a bar to good work and to the attainment of greatness. The world is not going backward in spite of its long-continued use of alcohol and so far as its use is concerned is in no danger of doing so.

There can be no doubt that there are many individuals who, while abstaining from alcohol themselves and believing against its use, are opposed to the manner in which national prohibition was brought about.

Porter<sup>16</sup> from clinical observations is convinced that many lives have been saved by the use of alcohol in cases of illness. Anything which interferes with this use of the drug is, he believes, to be deplored.

Newlis<sup>17</sup> pleads for less restriction to the physician in the use of alcohol. His conclusions as to the medical use of alcohol are as follows:

1. Many old persons have taken a certain amount of alcoholic stimulants each day for several years.
2. Intoxication is rarely seen in the aged.
3. When ill, no matter what the cause, the aged should take their regular amounts.

<sup>13</sup> Bull. de la Société méd. d. hôp., July 17, 1920.

<sup>14</sup> Boston Medical and Surgical Journal, August 12, 1920.

<sup>15</sup> New York Medical Journal, April 3, 1920.

<sup>16</sup> Ibid.

<sup>17</sup> Medical Review of Reviews, December, 1919.



4. It is often disastrous to discontinue an old man's habit, even if it is a bad one.

5. Whisky, beer or wines will improve digestion in the aged. Also they are of great value in the prostration attending senile pneumonia, nephritis and diabetes.

6. Must be used in its full physiological action. Physicians ordinarily use too small a dose.

7. Of great value in some cases of diphtheria with sepsis; alcohol has saved many patients after large doses of antitoxin have failed.

8. Alcohol taken for the relief of an acute disease will not form a habit.

9. Alcohol should be administered with food.

10. Of great value in senile debility and will relieve many symptoms like sleeplessness, numbness, cramps, etc.

11. "Wine is the milk of old age."

12. Alcohol is indispensable in treating many of the maladies of old age.

13. Legislation should not interfere with doctors obtaining alcohol for their patients.

One of the most serious results arising from the enforcing (?) of prohibition has been the frequency of *poisoning from wood alcohol*.

Although there is not a striking difference between methyl alcohol (wood alcohol) and ethyl alcohol, the method of preparation is distinctly different. Methyl alcohol is obtained by means of the destructive distillation of wood, while ethyl alcohol is obtained from the fermentation of grains or fruits.

For some reason wood alcohol seems to have a particular affinity for the optic nerves and many individuals have been partially blinded when the dose was insufficient to cause death. In the fatal cases there is usually coma, with death from respiratory paralysis. Whereas ethyl alcohol is completely oxidized with ease by the animal metabolism, wood alcohol is eliminated very slowly from the body. One of the end-products of its oxidation in the body is formic acid. As a result of the accumulation of formic acid, the condition known as acidosis may occur as the result of the ingestion of wood alcohol. Cases have been reported in which the drinking of wood alcohol was attended with marked cyanosis and severe air hunger or the hyperpnea of acidosis.

It need hardly be said that the drinking of any alcoholic drink at the present time is not altogether free from danger inasmuch as wood alcohol may be so prepared as to be ordinarily indistinguishable either by odor or taste from ethyl or grain alcohol.

Hubbard<sup>18</sup> warns against the danger of promiscuous drinking and especially of brews made by persons not familiar with compounding beverages.

It is to be borne in mind that trade names such as columbian spirits, cologne spirits, colonial spirits, standard wood spirits, union spirits, eagle spirits, greenwood spirits, Hastings spirits and acetone alcohol, purified alcohol and others, are names for methyl alcohol or wood alcohol in common parlance.

Scott and Hanzlik<sup>19</sup> have reported a group of cases poisoned by alcohol "denatured" with nitrobenzene. They state that "a large number of dark, ghastly-looking patients, who had been drinking denatured alcohol, were brought into the Hospital within a few days." As a rule, they were unconscious. The extremities, face, neck, including a fringe of the upper portion of the chest, was of a dark, almost black, color. In other words, the richly vascular, pigmented and dependent portions of the body were principally involved. The color was not the typical blue of ordinary cyanosis, but rather a livid, brown-black, or nearly black, suggesting the presence of methemoglobin in the blood, except for the deep narcosis and a moderately rapid pulse the patients were otherwise practically normal. There were no circulatory and no respiratory disturbances. After a deep sleep lasting about twenty-four hours, the patients left the hospital fully recovered. There were no untoward after-effects and no fatalities.

Examination of the blood showed the presence of methemoglobin. Examination of the "alcohol" showed an absence of methyl alcohol and the presence of formaldehyde. The presence of nitrobenzene was also demonstrated. Scott and Hanzlik believe that their study of these cases indicate that the dark discoloration, referred to above, was due to methemoglobinemia arising from the ingestion of nitrobenzene in the "denatured alcohol." The narcosis was due to the alcohol while the toxicity was due to the low concentration of formaldehyde. Although the poisoning was slight and non-fatal, they believe that there is considerable potential harm from such beverages where used over long periods, confusing at the same time the diagnosis of minor maladies.

Herrop and Benedict<sup>20</sup> report a case of *wood alcohol poisoning associated with acidosis*. The case was that of a woman who drank about half a pint of fluid supposed to be brandy. Subsequent examination of this fluid showed it to be wood alcohol. The following day the patient began to notice dimness of vision, pain in the back, headache, marked thirst and difficulty in breathing. On admission to the Hospital, the patient was drowsy and cyanotic, and breathing very deeply and rapidly. Gastric lavage was done and alkali administered by mouth, but this was not retained. As the air hunger (hyperpnea) rapidly grew worse, she was given 400 c.c. of a 5 per cent. sodium bicarbonate solution intravenously. Two days after the ingestion of the alcohol, vision was practically gone. The hyperpnea was less marked although the determination of the blood plasma bicarbonate still indicated a marked acidosis. A second intravenous injection of 500 c.c. of a 5 per cent. sodium bicarbonate solution was given and thereafter there was no evidence of acidosis either from examination of the plasma or symptomatically.

The vision gradually improved and the patient recovered.

As a result of their study, it was shown that there was an increase in the amount of titrable organic acids in the urine, and specifically with a marked increase in the excretion of lactic and of formic acids. They believe that the acidosis, when present, furnishes an indication for the

<sup>19</sup> Journal of the American Medical Association, April 10, 1920.

<sup>20</sup> Ibid., January 3, 1920.

use of prompt therapeutic measures. On the basis of their experience in this case they recommend that gastric lavage should probably be done over a period of several days. As already stated, one of the most serious effects of wood alcohol poisoning is the disturbance of vision due to involvement of the optic nerve.

Harboe,<sup>21</sup> in reporting a case of blindness following the drinking of spirits containing pure methyl alcohol, cites cases from the literature in which 11 cases of retrobulbar neuritis seemed to be due to wood alcohol. All other possible causes were excluded.

Fenton,<sup>22</sup> in reporting a case in which vision had been reduced to the perception of large objects, recommends the use of *dionin*. The case was seen four days after the taking of the wood alcohol. A solution of dionin (5 per cent.) was instilled into each eye, with the usual reaction of smarting and swelling of the conjunctiva. The aching previously complained of was much less in an hour's time. The patient was ordered to take sodium bicarbonate freely by mouth and told to instill the dionin daily for three days.

At the end of the three days, the vision was 20/20 right, 20/15 left. The patient stated that on awakening in the morning following the first use of the dionin she saw all objects fairly clearly but tinged with red; in an hour's time they had turned green, and by afternoon had resumed normal colors. The use of dionin was continued for three days in each week. Fenton believes that it is not unlikely that some postneuritic atrophy may follow and again reduce the vision somewhat, because the retinal edema is still present, though much diminished.

Fenton states that this instant local lymphagogue action of dionin is not dangerous, although the smarting and redness are uncomfortable for a short time. It is his hope that prompt use of a 5 per cent. solution of dionin may be made in other cases of wood alcohol poisoning, even if it is not immediately possible for an oculist to examine them. He feels that any measure that affords a decongestive action to the poisoned optic nerves should find early if cautious employment.

**Amyl Nitrite.** Hare<sup>23</sup> states that the one fact about *shock* that seems to be pretty generally accepted is that the commonest condition is one in which there is a great relaxation of the arterial system, with accumulation of blood in the great vessels of the abdomen and thorax, associated with a low arterial pressure. The accepted method of treatment is that which strives to restore vascular tone and circulatory equilibrium. The two essential needs seem to be restoration of the circulatory balance and the maintenance of body temperature.

Ducastaing<sup>24</sup> proposes a method of combating shock which, apparently, is diametrically opposed to the standard methods of treatment. His contention is that while there may be intense engorgement of the central bloodvessels, this is in a large part due to peripheral vasoconstriction, and for this reason he advises the employment of inhalations of

<sup>21</sup> Abstract, Journal of the American Medical Association, May 29, 1920, p. 1552.

<sup>22</sup> Northwest Medicine, January, 1920.

<sup>23</sup> Therapeutic Gazette, July, 1920.

<sup>24</sup> La Presse Médicale, December 20, 1919.



amyl nitrite. In 2 cases which he reports, a fatal issue occurred, but Ducastaing is convinced that the patients died as the result of the severity of their injuries and not from shock.

In his opinion, peripheral vasoconstriction is characteristic of shock, and the removal of this factor by inhalations of amyl nitrite is distinctly advantageous.

**Antimony.** The use of *tartar emetic* in the treatment of *bilharziasis* (*Bilharzia hematobia* and *Bilharzia mansoni*) now seems to be an established fact. Of all the various substances tried in this infection, Fairley<sup>25</sup> states that the only known remedy of importance is tartar emetic. He states that the drug was apparently first used in the treatment of bilharziosis by McDonagh, but Christopherson, quite independently, proved its value, and it is largely to the latter that we are indebted for showing its beneficial results. The drug has now been employed by a sufficient number of competent observers to establish its value.

Christopherson claims that tartar emetic not only kills the parasites *bilharzia mansoni* and *bilharzia hematobia in situ*, but later kills the miracidia in the ova deposited in the tissues of man.

The criteria of cure adopted by those who have employed the drug are as follows: (1) Improvement in the general health of the patient and disappearance of vesical symptoms; (2) the disappearance of ova in the excreta or the passage of ova containing only dead miracidia. Observations on the eosinophilia have also been made, and there is an agreement that during treatment a rise in the eosinophilia takes place.

In order to obtain additional evidence as to the effect of the drug, Fairley submitted 3 cases to critical investigation. In addition to the usual studies, the cystoscopical appearance of the bladder and complement deviation tests were made before and after treatment.

One case received a total of 50 grs. of tartar emetic; the other two—30 gr. each. The initial dose was  $\frac{1}{2}$  of a grain dissolved in 10 c.c. of saline solution; this dose was increased  $\frac{1}{2}$  of a grain each dose until the physiological limit of tolerance was reached. The point of tolerance was estimated by the amount of drug which produced paroxysmal coughing and vomiting immediately after the injection. When this occurred, slightly smaller doses were given. The amount of each single injection varied from 2 to 3 grains in different cases. The injections were given every second day at least two hours after the last meal.

During the treatment of these 3 cases, they all lost weight, did not feel well and were easily tired. No local effects followed the intravenous injections unless the fluid escaped into the perivenous tissue, when a severe local inflammatory reaction occurred. This happened in 1 case only.

Taylor<sup>26</sup> states that his experience showed immediate beneficial results. There was a rapid disappearance of the blood and ova from the urine, disappearance or mitigation of the hypogastric and perineal pains and pain on micturition, improvement in the anemia, gain in weight, and a striking improvement in the general appearance and feeling

<sup>25</sup> Practice of the Royal Society of Medicine, November, 1919.

<sup>26</sup> Journal of the Royal Army Medical Corps, August, 1919.

of well-being in the patients. As yet he cannot discuss the ultimate results, as too short a time has elapsed since the treatment was stopped and the patients discharged from the hospital.

Cawston's<sup>27</sup> found that after the second or third intravenous injection the scalding and vesical pain usually disappears and the blood in the urine in a week or ten days. The disease is usually cured when the urine has been free from living eggs for from two to three weeks.

While it is generally agreed that the drug kills or inhibits the activity of the parasite, it is not clear, as yet, at what stage in the life history of the parasite this occurs, whether ovum, miracidium, or adult worm, or all three. Christopherson claims that the drug exerts a direct helminthi-  
cidal action on the adult worm but experimental proof of this is still lacking.

In regard to the dosage which is undoubtedly large, it may be said that it is not without risk. Indeed the high toxicity of tartar emetic has always been, as Taylor points out, a matter of serious concern to all who have employed it in the form of intravenous injections, especially in the treatment of bilharziasis, trypanosomiasis, and leishmaniasis.

Among the untoward symptoms which may occur, the most frequent are pharyngeal irritation and paroxysms of coughing. The following untoward symptoms were noted by Taylor:

Cough and pharyngeal irritation . . . . .	9 cases
Stiffness of neck and shoulder muscles . . . . .	4 "
Nausea . . . . .	3 "
Vomiting (slight) . . . . .	4 "
Diarrhea (slight) . . . . .	3 "
Headache . . . . .	2 "
Induration . . . . .	2 "
Pyrexia (to 103° F.) . . . . .	1 "
Giddiness (slight) . . . . .	1 "
Pains in body . . . . .	1 "
General pruritus . . . . .	1 "
Loss of weight . . . . .	1 "
Relapse of hematuria . . . . .	1 "

A fatal issue may occur. Knowles has recorded 5 deaths out of 20 cases of kala-azar treated with tartar emetic, and Archibald and Innes have reported a fatal case of bilharzia so treated. In the latter case no adult worms were found at the autopsy which would tend to confirm Christopherson's contention that the drug has a direct helminthi-  
cidal action. Although no worms were found the congested mucous mem-  
brane of the bladder contained large numbers of bilharzial ova. The liver and kidney cells and the tunica intima of the inferior vena cava showed fatty degeneration, fatty infiltration, changes which were attributed to the action of the tartar emetic.

On the other hand, an enormous amount can, at times, be injected without ill-effects. Thus, in a case reported by Daniels, 236 biweekly intravenous injections of tartar emetic were given in the course of two and a half years. The maximum dose was 2½ gr., and the quantity administered amounted to the enormous total of 550 grains. This patient was infected with the *trypanosoma rhodesiense*.

<sup>27</sup> Lancet, April 17, 1920.

Taylor believes that because of the benefit of antimony in the treatment of bilharziasis, trypanosomiasis, etc., and also because the risks of poisoning (sometimes fatally so) cannot be ignored, other forms of antimony should be sought with equal therapeutic effects and a diminished toxicity. As he points out, antimony and arsenic are very closely allied in their chemical characters, and the toxicity of the latter has been greatly reduced, without diminishing its therapeutic action, by the development of organic combinations, such as salvarsan and its substitutes.

Because of the danger of tartar emetic, Sir Leonard Rogers was among the first to try and develop a less toxic form of antimony. In 1916, he recommended sodium antimony tartrate (Plummer's salt). More recently he has employed colloid antimony sulphide intravenously in kala-azar. He found it effective in smaller doses, being retained in the blood longer than the soluble tartrates of antimony. Taylor believes that in view of the efficacy of the soluble tartrates (tartar emetic) in bilharziasis, as well as of the occasional danger arising from their toxicity, it is evident that colloid antimony sulphide given intravenously would be well worth trying in bilharziasis.

Macfil<sup>28</sup> has employed tartar emetic in 10 cases of *guinea-worm infection*. In all but one of the cases treated with intravenous injections of tartar emetic, even in small doses, the drug appeared to have a beneficial action. There was relief of the inflammation caused by the breaking of the worm, a healing of the sore without the previous removal of the worm, and a shortening of the duration of the affection. In most instances it was not possible to continue the injections as long as Macfil thought necessary, either because the patients left his locality or because they themselves concluded, perhaps prematurely, that they had been cured. In the cases which were longer under observation, it appeared as if the antimony had killed the guinea-worm in the body and allowed it to be absorbed.

Patrick<sup>29</sup> insists that though quinine, when given by mouth in the treatment of *malaria*, may arrest the development of periodical attacks, it does not, in many instances, eradicate the parasite. He, therefore, decided to try the effect of both *quinine bihydrochloride* and *antimony tartrate* intravenously, using 15 grains of the former and about 2 grains of the latter on eight successive days. In some instances he first gave three doses of quinine and then five of antimony. In others, the quinine was given on the second, fourth and sixth days and the antimony on the others. It is to be noted, however, that on the days on which the antimony was given, 30 grains of quinine sulphate were given by mouth. This, of course, makes the deduction as to the value of the antimony somewhat questionable.

Patrick believes that antimony should be given a thorough trial and that it should be thought of in case there is an idiosyncrasy to quinine.

The results obtained by Rogers<sup>30</sup> indicate that the antimony salts used

<sup>28</sup> Lancet, March 20, 1920.

<sup>29</sup> Journal of the Royal Army Medical Corps, 1920.

<sup>30</sup> Journal of the American Medical Association, August, 1920, p. 1605.



intravenously are of value in the treatment of *filariasis*. He warns, however, that the treatment must be prolonged, and, as the drug is highly toxic, care must be exercised. He feels that more experience is needed before the precise value of the treatment can be decided.

**Apothesine.** The favorable effects following the use of this drug in the treatment of *hyperemesis gravidarum* has led Levy<sup>31</sup> to employ it also in cases of *postoperative vomiting*. This new synthetic local anesthetic is of low toxicity and without habit formation.

Levy began using it in place of cocaine, in doses of  $\frac{1}{12}$  of a grain combined with liquid taka-diastase. Later he increased the dose, and found that in nearly every instance doses of from  $\frac{1}{8}$  to  $\frac{1}{4}$  of a grain were successful in relieving pregnant women of the nausea. The drug may also be given in elixir lactopeptine. Food may be taken five minutes after each dose.

Sutton,<sup>32</sup> from his experience with apothesine and novocaine, states that these two drugs are the ideal anesthetics for local use, and that of the two he is inclined to give the preference to apothesine. He has never had any ill-effects following the use of apothesine as a local anesthetic.

It has also been used for spinal anesthesia in place of stovaine. Duboff<sup>33</sup> reports a death following the use of apothesine as a spinal anesthetic. In a review of the literature, he found that reported deaths from spinal anesthesia bear a considerable similarity, regardless of the drug used (stovain, novocain, tropacocain).

**Arsenic.** The use of arsenic in the form of *arsphenamin* has become so general that it is well to bear in mind that untoward results are not infrequent. Generally speaking the intravenous use of the drug may be practiced in a number of cases without anything happening. Then a series of cases is encountered in which untoward effects are frequent, although as a rule trivial in their consequences. Occasionally, a fatal result occurs even when the most careful technic is followed. Why this should be is not clear but it is reasonably certain that it will happen ever so often.

Strathy, Smith and Hannah<sup>34</sup> have reported 58 cases of *delayed poisoning* following the use of arsphenamin and mercury. Forty-seven of these cases showed symptoms referable to the liver, jaundice, decreased digestive power and atrophy of the liver. Of this latter group, 8 died, and the autopsy showed marked atrophy of the liver. The earliest symptoms pointing to arsphenamin poisoning of the liver were, bile in the urine, albuminuria, loss of appetite and jaundice.

Dermatitis occurred in 8 cases, of which 5 were characterized with marked exfoliation; peripheral neuritis occurred in 2; edema was noted in 2. Albuminuria was noted in 50 per cent. of the cases. The onset of the symptoms in these cases seldom developed until five weeks had elapsed since the administration of the arsphenamin.

<sup>31</sup> Therapeutic Gazette, January, 1920.

<sup>32</sup> Ohio State Medical Journal, April, 1920.

<sup>33</sup> Journal of the American Medical Association, August 28, 1920.

<sup>34</sup> Canadian Medical Association Journal, April, 1920, No. 4, 10.

Dermatitis, with atrophy of the liver, occurred in one patient who received arsenic in the form of Fowler's solution, 5 minims, three times daily, for five months.

In the treatment of *Vincent's angina*, Theisen<sup>35</sup> states that arsenic in some form has almost a specific action in some cases. Salvarsan (arsphen-amin) locally and intravenously, in bad cases, is of great service and potassium iodide internally is a good adjunct to the local treatment. Theisen states that Halsted has had good results with the use of *enesol*, an arsenate of mercury used hypodermically.

Theisen has found that a strong solution of potassium chlorate, powdered alum, carbolic acid, glycerine and water is almost a specific in some cases, and clears up the throat lesions quicker than anything else. For adults and older children this solution is used as a gargle; for very young children it is used as a spray in strength corresponding to the age of the child. Bad teeth and diseased tonsils should be attended to. This solution should be used every half hour in severe cases and every hour or two in the milder cases. As the lesions begin to clear up, the solution can be used less frequently.

Theisen is of the belief that Vincent's angina is a fairly common condition, and, if looked for, will be found more frequently than is generally thought.

**Aspidosperma.** This drug has long been known in the treatment of certain chronic respiratory conditions. It is little used, and, although I have had no experience with it in recent years, my early experience with it was not especially favorable.

In writing on its use, Wilcox<sup>36</sup> states that he has often obtained brilliant results and occasionally equally inexplicable failures. He recommends it in those conditions in which the respiratory act is embarrassed, as in emphysema, chronic bronchitis or chronic pneumonia. He states that it will often give instant relief. It appears to assist the oxygenation of the blood, as well as to stimulate the respiratory center. It is often of great service in symptomatic asthma (dyspnea) when due to uremic conditions and at times when due to heart failure. He thinks that it is probable that when the dyspnea is not symptomatic of a serious organic lesion the effects of the remedy will be constant and satisfactory. It is not curative, but possesses a marked action in presenting a recurrence of the attacks. After its administration there is usually a feeling of warmth in the head, some perspiration, and frequently slight salivation. The dose of the fluid extract required for this purpose is from  $\frac{1}{2}$  to 1 teaspoonful every two to four hours. If too long continued it is apt to cause nausea.

*Aspidospermine* represents fairly well the activity of the drug with the further advantage that it may be used hypodermically in a dose of 0.2 grain.

**Belladonna.** Belladonna, or its alkaloid *atropine*, has long been employed in certain types of indigestion, notably those associated with a

<sup>35</sup> Albany Medical Annals, July, 1919.

<sup>36</sup> Medical Record, October 25, 1919.

hypersecretion of hydrochloric acid. Bastedo<sup>37</sup> apparently does not credit the drug with much beneficial action under these circumstances. He states that in the ordinary hyperacidity case, with cessation of secretion at the usual time, atropine or belladonna, in maximum doses, either by mouth or hypodermically, has no useful effect on acidity or secretion. In hyperacidity cases atropine had no useful effects in any dosage. In continuous hypersecretion cases, the drug may check the secretion after the digestive period, but it does this in maximum doses only. In pylorospasm it may be useful, but in maximum doses only. In the doses usually employed, it is wholly without effect on the secretory or the motor function of the stomach.

Notwithstanding these results, I have often given relief to patients apparently suffering from oversecretion by the use of belladonna in small doses after meals.

Hass<sup>38</sup> believes that *atropine* is extremely valuable in the treatment of *pylorospasm* and *pyloric stenosis*. He thinks that the drug should always be given a trial before resorting to surgical measures as it may effect a cure. He thinks that the use of atropine is the logical treatment in these cases owing to its paralyzing effects upon the vagus nerve endings. Hass emphasizes the following facts regarding atropine: (1) the inconstancy in value in which it resembles digitalis; (2) its rapid deterioration; (3) it must be used in sufficient dosage to be effective.

A common dose of atropine for an infant from a few weeks to a few months of age totals  $\frac{1}{50}$  to  $\frac{1}{25}$  gr. in twenty-four hours, with an extreme of  $\frac{1}{16}$  of a grain divided among the day's feedings. A 1 to 1000 solution is used, beginning with one drop and increasing rapidly until effective. The most frequent toxic symptoms are flushing, mydriasis and dryness which disappear promptly when the drug is withdrawn. Hass states that there is no danger, even when untoward symptoms occur. While it is true that young children are, as a rule, especially tolerant to belladonna, these doses, Hare remarks, are heroic for an infant. Haas states that the principal argument against the medical treatment of these cases is the sudden death which sometimes occurs. These, he states, are thymus deaths, and occur in cases operated upon as well as those medically treated.

**Benzol.** Benzol was employed quite extensively a few years ago in the treatment of *leukemia*. It is little used for this purpose at the present time. The chief objection to its use is that in curtailing the production of the white cells it may so affect the bone marrow as to aggravate the patient's condition rather than improve it.

Revenua,<sup>39</sup> in reporting 3 cases of chronic myeloid leukemia in which benzol had been employed, states that it is purely a symptomatic remedy and must be applied with extreme caution. The symptoms inevitably return sooner or later, and often in a more severe form. A necropsy was obtained in 2 of the cases. There was nothing found which indicated any injury resulting from the benzol nor was there an accumulation of leukocytes in any organ.

<sup>37</sup> American Journal of the Medical Sciences, January, 1920.

<sup>38</sup> New York State Journal of Medicine, October, 1919.

<sup>39</sup> Riforma medica, January 24, 1920.



The use of benzol in industry has led to cases of *poisoning* from its use. Legge<sup>40</sup> has reported 2 cases of *purpura hemorrhagica* in rubber spreaders. The symptoms were practically identical in both cases. The trouble started with malaise and submucous hemorrhages and both cases were admitted to the hospital because of bleeding from the nose, gums, and bowels. The blood-count in one case was: red cells, 2,800,000; leukocytes, 2000; hemoglobin, 35 per cent. The chief characteristics found at the necropsy were numerous submucous hemorrhages throughout the intestines and under the endothelium of the heart. In the second case characteristic changes were found in the marrow of the long bone. The conditions observed during life and after death were those seen in cases of aplastic anemia and are identical with those which have been noted in fatal cases arising from poisoning by T. N. T. may produce the same condition.

The therapeutic use of benzol is in cases of leukemia which occurs in cases of industrial poisoning, namely, the serious impairment of the bone marrow function and the promotion of an aplastic anemia.

**Benzyl Benzoate.** This opium derivative, introduced by Macht, was reviewed *in extenso* last year. It will be recalled that the drug is supposed to be non-toxic and to have a definite antispasmodic action on unstripped muscle fibers. Boice,<sup>41</sup> from his experience, concludes that while the results so far attained do not seem to be more than relatively conclusive, the apparent non-toxicity of the drug seems to warrant a more extended and thorough trial at the hands of the profession. He recommends, therefore, that where an antispasmodic of the opium type is indicated, for its relaxing action on unstripped muscle fiber, that benzyl benzoate be given a thorough trial. It seems to be indicated particularly in conditions such as dysmenorrhea, asthma, diarrhea, arteriosclerosis and esophageal and pyloric strictures.

Macht<sup>42</sup> has used benzyl benzoate with excellent results in the treatment of *hiccup*, not only in the ordinary form encountered in infants, but in the type which is persistent and often termed pernicious. He states that the action is best exerted when given in a 20 per cent. solution in alcohol. Of this solution the patient is given from 20 to 40 drops in water or milk. Macht does not recommend the use of the drug in suspension in various elixirs or syrup, as it has no advantage. He disapproves of giving the drug in capsules as in some instances it may produce local irritation, and in others render the action too slow. In children, the alcoholic solution may be conveniently administered in sugar, water or milk.

In addition to its therapeutic value, Macht believes that the benzyl benzoate is of diagnostic value in differentiating between the hiccup of central origin and that due to some peripheral irritation. Inasmuch as benzyl benzoate exerts its chief effect peripherally on the smooth muscle structures, Macht is inclined to believe that the drug may be most useful in the treatment of hiccup of peripheral origin.

<sup>40</sup> Journal of Industrial Hygiene, March, 1920.

<sup>41</sup> New York Medical Journal, December, 1919.

<sup>42</sup> Medical Record, July 24, 1920.

McMurray<sup>43</sup> has employed benzyl benzoate in the treatment of *whooping-cough*. He gave from 5 to 30 minims, depending on the results. In some cases, decided improvement was noticed from the smaller doses, while in others, large doses were required. In nearly every instance there was a lessening of the severity of the paroxysms. The effect of the drug was manifest within forty-eight hours. As a rule, the relief was immediate and complete. No untoward effects were noted. A child of twelve months of age was given 20 minims with no evidence of trouble.

In a study of 115 cases of *whooping-cough* in which benzyl benzoate had been administered, Macht<sup>44</sup> found that about 90 per cent. of the patients showed more or less beneficial effects; about 50 per cent. exhibited marked improvement in the symptoms. Most of the patients before coming under observation had been given paregoric and other popular drugs, and some had been treated with vaccine. Macht stopped all medication and gave from 5 to 40 drops of a 20 per cent. solution of benzyl benzoate by mouth three or four times daily; or oftener depending on the age of the patient and the severity of the attack.

In cases in which the simple alcoholic solution was found to be distasteful to the younger patients the solution was flavored with a few drops of benzaldehyd and then given in sugar, water or milk. Macht found that the addition of a little benzaldehyd to a solution of benzyl benzoate in amounts varying from 1 to 5 per cent. produced a mixture which seemed to be more effective than the benzyl benzoate alone. Trying to disguise the taste by means of various elixirs and syrups did not succeed very well.

The drug has no curative effect on the *whooping-cough* but is distinctly valuable as a palliative.

In order to overcome the bitter, burning taste of the benzyl benzoate, Hirschfelder<sup>45</sup> recommends the following formula:

Pure benzyl benzoate . . . . .	10 parts
Emulsion of acacia . . . . .	5 "
Elix. eriodictyon aromaticum (N. F.) . . . . .	35 "

Dose one tablespoonful.

He states that the drug brings relief in many, but by no means all, cases of *asthma*. His most striking results have been obtained in the treatment of *dysmenorrhoea*; about 80 per cent. of this group were relieved of their pain after from one to three doses.

The fact that benzyl benzoate is a powerful vasodilator without being a cardiac depressant, has led Macht<sup>46</sup> to employ the drug in the treatment of *hypertension* and *angina pectoris*. He employs a 20 per cent. alcoholic solution, in cold water or milk, in doses of 20 to 30 drops, three or four times a day. After the full effects of the drug are obtained, the pressure may be kept at a satisfactory level on doses of 5 drops of the alcoholic solution. The effect of benzyl benzoate on the blood-pressure was demonstrated when other methods had failed to produce a vasodilatation.

<sup>43</sup> New York Medical Journal, July 24, 1920.

<sup>44</sup> Bulletin of Johns Hopkins Hospital, April, 1920.

<sup>45</sup> Minnesota Medicine, August, 1920.

<sup>46</sup> New York Medical Journal, August 28, 1920.

In an experimental study of benzyl benzoate, Heller and Steinfield<sup>47</sup> found the drug to be without toxic effects on the leukocytes of rabbits. They believe there is a wide margin of safety between the therapeutic and toxic doses of benzyl benzoate.

**Betanaphthol.** Smilie<sup>48</sup> concludes from his experience that this drug is unsafe in the treatment of *hook-worm disease*. In 79 cases in which large doses were used (18 gm. for adults) severe toxic symptoms occurred in 2 cases and in 2 others, marked changes in the blood-cells were noted. The toxic action of the drug in these 4 cases manifested itself in a destruction of the red blood-cells, which occurred in great numbers. This resulted in severe anemia, jaundice, enlargement of the spleen and liver, enlargement of the gall-bladder and hemoglobinuria. The white cells apparently were unaffected. The type of case most susceptible to the toxic action of the betanaphthol was not determined but all of the cases affected gave a history of recent malaria. It is possible that the malaria made the red cells more fragile and as a result more susceptible to the betanaphthol.

Hare, in commenting on Smilie's results, states that any drug which tends to destroy the red cells would seem to be contra-indicated in a disease which causes anemia.

**Camphor.** This drug is frequently employed in cases where a rapidly acting heart stimulant is needed; it is often used in certain of the acute infections, such as *pneumonia*, to avert threatened cardiac failure. Bryan<sup>49</sup> has employed camphor hypodermically in the treatment of pneumonia not as a heart stimulant but for the purpose of overcoming the toxemia and killing the pneumococci.

As soon as the diagnosis of pneumonia is established, Bryan gives to an adult  $2\frac{1}{2}$  mils of a solution of camphor and olive oil. Each mil of the solution contains  $2\frac{1}{2}$  grains of camphor. He gives four doses daily. If the patient is not seen until the fourth or fifth day, or the case is unusually severe, the injections may be continued for one or two nights. He states that poisoning is not likely to ensue.

About the third day after the camphor has been given, the rusty sputum is replaced by whitish and mucopurulent sputum and the temperature begins to fall. In his series of 12 cases, the temperature was normal by the fourth or fifth day and the patient felt comfortable after the second day.

The camphor is first dissolved in ether or chloroform and then mixed with the best grade of olive oil, not cottonseed oil. It is then poured into half ounce bottles and sterilized by boiling. Cotton plugs are put in the mouth of the bottles and the bottles are then placed in a water-bath. The corks are boiled separately. The sterilization takes from one-half to an hour.

Bryan advises the smallest hypodermic needle. Hare points out that olive oil will not pass through very small needles, but almond oil will.

The injections are best made by lifting up a fold of skin and inserting

<sup>47</sup> New York Medical Journal, July 31, 1920.

<sup>48</sup> Journal of the American Medical Association, May 29, 1920.

<sup>49</sup> China Medical Journal, September, 1919.



the needle so that it will go through the skin, fascia, and fat, and distribute the oil between the fat and the muscle. Bryan states that it is the needle plunging into the muscle that gives rise to pain and causes a lump to appear afterward. The injections should be made at different points: right triceps, left triceps, outside of thighs, etc.

H. R. Miller<sup>50</sup> has found that the local action of drugs, notably adrenalin, and local anesthetics, such as procain, exhibit a strikingly prolonged drug effect when administered subcutaneously and in an oil vehicle. In this way it has been possible to use adrenalin in oil for clinical conditions such as *bronchial asthma*, certain *urticarial eruptions* and in certain types of *pneumonia*. Giving the drug in oil establishes a local subcutaneous depot of adrenalin in oil and thus procures rather continuous adrenalization effects by repeating the subcutaneous injection every eight to twelve hours.

Experimentally, Miller was able to give the oil intravenously to dogs in doses of 10 c.c. without noticeable ill-effects. In man, oil was administered intravenously in doses of 0.25 to 1.5 c.c. in a small group of cases. Although he states that there were no signs or symptoms of emboli, I should hesitate to employ oil intravenously. The drugs he has so far experimented with in oil are adrenalin, mainly, crystalline strophanthin, nitroglycerine and pituitary extract.

Mock and Wander<sup>51</sup> caution against the employment of a mineral oil for subcutaneous injections. This fact has been well established in regard to paraffin injections, and the tumors resulting from the injection of camphor incorporated in mineral oil strengthens the conclusion.

**Cerium Salts.** In recent years the hope of securing a specific treatment for *tuberculosis* has centered in chemotherapy. In this connection it is to be borne in mind that in no field of experimental endeavor is patience more needed. Above all to be deplored is the tendency to prematurely try clinically substances that show little more than an interesting lead. This remark is inspired by the recent publicity which the lay press has given to the treatment of tuberculosis with the salts of cerium.

Three articles on the use of these salts have recently appeared in one of the French Medical Journals, namely—one by Grenet and Droum, one by Rénou and one by Esnault and Brou.<sup>52</sup>

An editorial criticism<sup>53</sup> on these articles is as follows: "A few observations of the inhibitory activity of salts of cerium, and some other rare earth metal (especially samarium, neodymium and praseodymium) were made on the growth of tubercle bacilli in cultures, possibly because they are rare substances and had not yet been shown to be valueless in tuberculosis. According to the figures given, the inhibitory action of these salts is not at all high, about one to five parts per thousand being required to prevent growth, which may be contrasted with gold chloride, which inhibits when in dilution of 1 to 2,000,000, and yet which

<sup>50</sup> Journal of the American Medical Association, May 1, 1920.

<sup>51</sup> Archives of Dermatology and Syphilology, March, 1920.

<sup>52</sup> Bull. de la Soc. méd. de hôp., May 7, 1920.

<sup>53</sup> Journal of the American Medical Association, July 24, 1920.

in the careful studies of De Witt, as in the earlier observations of Koch, could not be made to show any favorable influence on tuberculosis in animals. As far as we can learn, no attempts were made to determine the capacity of the salts of the rare earths to kill tubercle bacilli, and there is no report made of any systematic study of their effects on experimental tuberculosis in animals, in which alone can accurate controls be made. These cases, less than a hundred in the reports published, have now been observed at the most a few months, and it is believed that cutaneous glandular, and chronic afebrile tuberculous pulmonary lesions have been improved, and that patients with active pulmonary tuberculosis have been made worse. There is no mention of control patients given the same general care without the salts." The writer of the editorial recalls that many other substances, now long forgotten, have had as much exploitation and then passed out of sight. The writer furthermore entirely disagrees with Rénou who states that: "The results obtained by Grenet and Droum with the sulphate of the cerium earths are certainly the most scientific yet realized in the chemotherapy of tuberculosis."

Of the justice of the above criticism, there can be no doubt in the minds of those who have seen any number of methods of treatment similarly praised and then finally become forgotten.

**Chaulmoogra Oil.** A chemotherapeutic study of the chaulmoogra oil series and other fatty acids in *leprosy* and *tuberculosis* has been made by Walker and Sweeney.<sup>54</sup> They state that chaulmoogra oil contains bactericidal substances that are about one hundred times more active than phenol. These bactericidally active substances are the fatty acids of the chaulmoogra series, chaulmoogric and hydnocarpic acids, and possibly lower isomers of this series. They found the chaulmoogra acid series to be specific for the acid-fast group of bacteria, and inactive against all other bacteria tested.

This specific bactericidal activity against acid-fast bacteria is a function of the carbon ring structure of the molecule of the chaulmoogric acid series which, so far as known, is found only in chaulmoogra oil and in oils closely related to Tara-ktogenous Kurzii.

These facts, they think, supply a scientific basis for the use of chaulmoogra oil and its products in leprosy. Furthermore, the bactericidal activity of the chaulmoogric acids against all members of the acid-fast group of bacilli, together with the clinical results obtained in the treatment of leprosy, furnish theoretical grounds for the use of the chaulmoogrates in the treatment of tuberculosis.

Walker and Sweeney do not believe that the fatty acids of *cod liver oil*, the salts of which constitute Roger's *sodium morrhuate* used in the specific treatment of tuberculosis do not possess the specific bactericidal activity of the chaulmoogric acid series.

Muir<sup>55</sup> has analyzed 300 cases of leprosy treated with *sodium hydnocarpate* and sodium morrhuate. In this series 179 were of the anesthetic type, 81 of the mixed and 40 of the nodular or tubercular type. The

<sup>54</sup> Journal of Infectious Diseases, March, 1920.

<sup>55</sup> Indian Medical Gazette, April, 1920.

dosage of both drugs varied from  $\frac{1}{2}$  c.c. to 5 c.c. of a 3 per cent. solution, beginning with the smaller dose and gradually increasing. The sodium hydnocarpate was given chiefly intravenously while the sodium morrhuate was given subcutaneously, intramuscularly and occasionally intravenously.

The sodium hydnocarpate was much the most effective; of the patients treated with it 132 were improved, 58 were greatly improved and in several the lesions entirely disappeared. With the sodium morrhuate 33 were not improved, 48 were slightly improved and 36 were much improved. None were made worse.

Muir believes that the best results are obtained in the anesthetic cases with sodium hydnocarpate but veins soon become blocked and sodium morrhuate must then be resorted to as it can be given subcutaneously or intramuscularly. In the nodular type both drugs seem to be equally efficacious.

Neve<sup>56</sup> finds that in the treatment of leprosy with *sodium gynocardate* and sodium morrhuate about half the patients appear to be benefited in six months. Those not definitely improved remain stationary. Only about 10 per cent. show fresh lesions while undergoing the treatment. Neve states that one must be cautious in employing these remedies when laryngeal or ocular leprosy is present.

Rogers<sup>57</sup> has continued his use of the cod-liver salts in the treatment of tuberculosis. He now employs an ethyl ester morrhuate. While he believes that the treatment is of value further experience is needed to establish his claim.

Gonguli,<sup>58</sup> from his experience with sodium morrhuate in the treatment of tuberculosis, is convinced that it is of value. As already stated Walker and Sweeney could find no evidence of the value of sodium morrhuate in the treatment of conditions caused by acid-fast organisms.

**Chenopodium.** Of recent years this drug has gained a wider reputation in the treatment of *ankylostomiasis*. Wrench,<sup>59</sup> in an investigation of the drugs commonly employed in this condition, concludes that the cures so frequently reported and in such large numbers, are not justified if by cure is meant freedom of the stools from ova. He states that chenopodium oil is a dangerous drug. In 151 treatments, there were 32 instances of vomiting, many cases of giddiness and occasionally slight collapse. On nine occasions, two capsules could be given as a treatment, and on one occasion one capsule only could be given. In Wrench's opinion, *thymol* is inferior to chenopodium, and as a means of sterilization is unreliable.

**Chlorine.** Barbour and Williams,<sup>60</sup> in a study of the effects of chlorine on isolated bronchi and pulmonary vessels, state that even small concentrations lead to a slight relaxation of pulmonary vessels. Stronger concentrations lead to contractions but these vascular rings will, however, relax again if the solution be replaced by one which is chlorine-free. The bronchial musculature yields similar effects to chlorine but the

<sup>56</sup> Indian Medical Gazette, April, 1920.

<sup>57</sup> Ibid.

<sup>58</sup> Ibid.

<sup>59</sup> Indian Journal of Medical Research, January, 1920.

<sup>60</sup> Journal of Pharmacology and Experimental Therapeutics, September, 1919.



relaxation occurs with less constancy. Another difference between the pulmonary vessels and the bronchi lies in the fact that for the latter the minimal constricting concentration is much lower than the former.

Barbour, Hjort and Taylor<sup>61</sup> state that subcutaneous doses of morphine as large as 10 mg. per kilogram (twice daily) exert, if anything, an unfavorable effect on chlorine-gassed dogs. Smaller doses (3 to 5 mg.) have little effect on the fatality percentage but it would appear that morphine may safely be used on gassed individuals, for its analgesic effect, if the size and frequency of the doses are limited.

In the treatment of gassed individuals, Barbour<sup>62</sup> believes that an excessively warm environment may be as dangerous as one which is too cold.

**Colchicum.** Inasmuch as *gout*, especially the acute form, is not often seen in this country, the need for colchicum is not great. At the same time, acute cases are being encountered from time to time and it is well to remember that the drug is almost a specific in this disease. Matthews,<sup>63</sup> while admitting the value of the wine and the tincture of colchicum, has found the acetic extract the most effective preparation.

The dose recommended, namely,  $\frac{1}{4}$  to 1 grain (B. P.), he thinks is too small to be effective. In his opinion, the dose should be from 2 to 6 grains. In his hands it has proved safe in the following<sup>\*</sup> prescriptions:

R—Pulv. opii . . . . .	gr. j
Pulv. ipecac. . . . .	gr. j
Pulv. cambog. . . . .	gr. ij.
Pulv. aloes . . . . .	gr. iv
Ext. colchici acet. . . . .	gr. viij

M. et ft. in pil., div. in 4. Mitte 12 or 24.

Sig.—One pill three times a day, or two at night and one in the morning.

This combination rarely, if ever, fails to relieve rapidly and completely all the symptoms, especially in the acute cases.

**Corpus Luteum and Ovarian Extract.** Quigley<sup>64</sup> has treated 17 cases of *vomiting of pregnancy* with 12 permanently benefited; 4 were benefited but relapsed, owing to insufficient dosage; and in one case there was complete failure. He employed 1 c.c. ampoules containing 0.2 gm. of the desiccated substance of the gland. The number of doses ranged from four to thirteen and with one exception were given hypodermically. Welz<sup>65</sup> has used the desiccated corpora lutea in 38 women suffering more or less from the toxemia of early pregnancy. He employed a solution equivalent to 2 grains of desiccated corpora lutea in 1 c.c. of physiologic salt solution saturated with chloretone for the local anesthetic effect. This comes prepared in ampoules in sterile solution ready for use.

A special effort was made not to permit suggestion to play any part in the treatment. In the clinic cases, injections were given without a word as to their purpose. As other routine measures, such as drawing blood for the Wassermann test, were made, the patient received the

<sup>61</sup> Journal of Pharmacology and Experimental Therapeutics, September, 1919.

<sup>62</sup> Ibid.

<sup>63</sup> British Medical Journal, August 30, 1919.

<sup>64</sup> New York State Journal of Medicine, August, 1919.

<sup>65</sup> Journal of the Michigan State Medical Society, July, 1919.

injections without knowing or suspecting what they were for. The results were gratifying in all of the 38 cases, except one complicated with Graves' disease. There was a slight recurrence in 16 cases, but these responded quickly after the administration of from one to three injections. In mild cases there was usually an improvement after the first or second injection, and almost complete alleviation of the nausea after the third or fourth injection. Three severe cases responded to a course of injections given twice daily; all were confined to bed and unable to retain any food.

Welz reaches these conclusions:

1. During early pregnancy there is a great increase in corpus luteum and also in the internal secretion from it.

2. A deficiency in the normal increased secretion from the corpus luteum of pregnancy results in a toxemia of early pregnancy.

3. The principal symptoms of this toxemia are nausea and vomiting. Others less common are dizziness, headache, vertigo, neurasthenia, insomnia, mental depression. Later the symptoms of undernutrition and emaciation follow.

4. The administration of the extract from corpus luteum corrects these symptoms by supplying the deficient secretion of corpus luteum in the individual suffering from this toxic state.

5. The regular exhibition of this extract may control cases of habitual abortion due to deficient corpus luteum development in early pregnancy.

6. Diagnosis of early pregnancy may occasionally be aided by the specific effect of corpus luteum extract in stopping hyperemesis.

Clagett<sup>66</sup> also speaks highly of corpus luteum in the treatment of the nausea and vomiting of pregnancy. In five instances this treatment averted the only alternative left, namely, a therapeutic abortion. He has also used corpus luteum with good results in *menorrhagia*. In these cases one ampoule is administered every three days over a period of several months. A new ovarian preparation has been placed on the market which is made from the residue of fresh ovaries after ablation of the corpus luteum. It is a grayish powder and is supplied in tablets of 5 and 10 grains each. Clagett states that the removal of the corpus luteum makes this residue most suitable in cases of oligomenorrhea and sexual inactivity. He has employed it with success in both instances. Graves<sup>67</sup> has employed the ovarian residue in 41 cases of artificial and natural *menopause*, most of which showed a marked amelioration of the symptoms. He has also had excellent results in 24 cases of *amenorrhea*, delayed or scanty menses and 28 cases of dysmenorrhea.

The ovarian residue (ovarian substance with the corpora lutea removed) seems to be especially indicated in cases of sterility and repeated abortion.

In Novak's<sup>68</sup> opinion, *functional uterine bleeding* is not due to primary disease of the endometrium but is secondary to an endocrine disturbance of the ovary. This type of bleeding, occurring without gross pelvic dis-

<sup>66</sup> Therapeutic Gazette, May, 1920.

<sup>67</sup> Surgery, Gynecology and Obstetrics, December, 1919.

<sup>68</sup> Journal of the American Medical Association, July 21, 1920.

ease is very common at the menopause, when it often leads to the suspicion of malignancy. It is next most frequently observed at or near the time of puberty, but may occur at any age. It is usually of the type seen in cases of menorrhagia, with not infrequently, periods of amenorrhea. Novak has tried thyroid therapy in these cases, with disappointing results. The administration of ovarian extracts, and especially of those derived from the corpus luteum seem to be of value, at times, but the results are anything but constant.

Oginz,<sup>69</sup> in commenting on the value of ovarian extracts in the treatment of ovarian dysfunction, emphasizes the necessity of thoroughly investigating the patients' condition in order to eliminate pelvic inflammatory conditions in their active state, new growths, uterine displacements, etc. It is necessary to exclude pathological conditions, as the ovarian extract will certainly fail in their presence.

In the management of *hypertension* in women, Riesman<sup>70</sup> states that he has secured apparently striking results from the use of corpus luteum extract. The blood-pressure is lowered without any untoward effects, and the subjective symptoms are markedly improved.

In young girls who develop simple goiters which are to be regarded as an effort on the part of the thyroid to compensate for ovarian deficiency, the goiters rapidly disappear when ovarian substance is prescribed.

**Diet.** NUTRITION STUDIES. As the result of war conditions and the high cost of foodstuffs, the dietary of most people, particularly the poorer classes, has undergone marked changes. This has resulted in an unusual amount of attention being paid to dietetics. Nutrition classes are springing up everywhere and if one is to believe all that is said every evil to which the flesh is heir can be cured by a "scientific" diet. This has led to the development of a new type of social worker, the lay dietitian. As a rule, she is a young woman who has taken a brief course in dietetics, and, as a result of her three or four months training, is prepared to solve the whole problem. This class reminds me very much of a remark the late Phineas Connor made in regard to specialists whose training consisted of a three or four months course in one of the Polyclinics, namely, that they were dangerous in direct proportion to the number of patients they had. If these remarks seem too severe, it is to be attributed to repeated irritations from this new type of worker.

Several years ago I reviewed the work of Emerson, of Boston, on the building up of delicate children. He has called his classes, Nutrition Classes, a name which, I think, should be changed to Classes for Delicate Children. During the past year I organized a class of these children along the lines laid down by Emerson. I was able to confirm all that he has claimed. Children are delicate and undernourished for a variety of reasons. In about 60 per cent. there is some physical defect, such as diseased tonsils, adenoids, carious teeth or some chronic ailment. This must be removed before the child is free to gain. Another group is made up of children who are chronically fatigued. This may be due to working after school hours, or in the case of the Jewish children—of going from

<sup>69</sup> American Medicine, September, 1919.

<sup>70</sup> Journal of the American Medical Association, August 2, 1919.



the Public School in the afternoon to a two-hour session of instruction in Hebrew. In another group the child has faulty dietary habits, eats too fast, or is irregular.

Finally, the food itself may be at fault; either it is insufficient or of a poor quality. As a rule two or more of the above factors are present. It can be seen that the problem of dealing with these children is essentially a medical one. A competent physician is needed to determine the nature of the defect and prescribe the course of treatment. It cannot be too strongly emphasized that it is not one of dietetics. Building these children up is not to be done by prescribing a well balanced diet.

The problem of dealing with these children has been made harder by the tremendous increase in the cost of articles of food which formerly were very cheap and easily obtained.

Langworthy<sup>71</sup> has made a study of the cost of foodstuffs purchased by 500 families and compared these prices with those expended by 400 families about twenty years ago. His results showed that the amount of meat in the diet has decreased about 8 per cent. and grain products about 11 per cent., while dairy products have increased about 6 per cent.; vegetables, 4 per cent.; and fruits 8 per cent.

Our experience at the Phipps Institute is not in accord with those of Langworthy in regard to milk. When I started the Class for Delicate Children referred to above, I found that milk, once the sheet anchor, was being used in smaller quantities than formerly. This was entirely due to the enormous increase in the price of even the cheapest grades of milk. Where formerly it was 5 cents a quart, it had jumped to 14 to 18 cents a quart. In this connection may be mentioned the milk scandal in New York City involving the charge that the price of milk for the poor was prohibitive and was being purposely kept up. An investigation of a number of our families at the Phipps Institute disclosed the fact that in every instance they were purchasing one-half the milk they did the year before. In addition, a number of samples obtained by us showed that, with one exception, the milk sold for these high prices contained one-half or less, the amount of fat it should, a similar and independent investigation by the Board of Health revealed the same thing.

As an adequate supply of milk was not obtainable for these children, we sought to substitute other foodstuffs to compensate for this milk deficiency. Some of our recommendations were published in the lay press. This aroused a storm of protest from the dairy interests, who asserted that we were trying to deprive children of milk, the most essential form of food they needed. As a matter of fact, we appreciated that every child needed some milk; what we were trying to do was to furnish a sufficient caloric intake with cheaper but equally nutritious foods.

As an example of what may be accomplished in the way of utilizing cheaper articles of food, mention may be made of an article by Johns and Finke<sup>72</sup> on the nutritive value of peanuts. The peanut is easily digested by man and has a high protein content. In experimental

<sup>71</sup> *Journal of Home Economics*, December, 1919.

<sup>72</sup> *Journal of Biological Chemistry*, July, 1920.

animals, a bread made of 25 parts of peanut flour and 75 parts of wheat flour furnished adequate proteins for normal growth. The proteins of the peanut bread were utilized for gain almost twice as well as those contained in wheat bread. While this does not mean that peanut flour alone or mixed with wheat flour should be a regular procedure, it does show the high nutritive value of the peanut. Twelve double peanuts equal 100 calories, and they can be used to advantage in building up the diet of a child in case the necessity of utilizing cheap but nutritious food arises.

Cereals are also too little used by the children of the poorer classes, especially the foreign born. In this connection it may be said that there has been some question as to whether all cereals were of equal value. This question has been investigated by Osborne and Mendel.<sup>73</sup> Contrasting wheat with barley, rye and oats in experiments in which these grains served as the sole sources of protein for growth, they found that the proteins of the four cereals studied are not widely different in efficiency. They state, however, that although the cereals may be equal from the standpoint of comparative protein values, they need to be supplemented, notably with specific inorganic elements and fat-soluble vitamin. From the physiologic standpoint they point out that the day of "invidious distinctions" seemingly is past.

It is a mistake to assume that the general prosperity has affected all individuals and that everyone is capable of meeting these tremendous increases. There is still a great deal of poverty and there are many children whose families are unable to obtain for them a large supply of milk. So long as this state of affairs continues, all that we can hope to do is to see that each child gets the minimum amount of milk needed and to build up the diet with other cheaper foods.

The cry that milk contains the most necessary of the vitamins is urged in favor of plenty of milk. The trouble at present is that no one knows certainly how much milk is needed to furnish this necessary ingredient. I have been told by dietetic experts that six ounces of milk are sufficient for this purpose. If this is true, a pint, certainly one quart, which we require, should be ample. Providing one can give children several quarts of milk daily, the problem of building them up is relatively easy if defects or other retarding influences are removed. In the meantime, we must be satisfied with smaller amounts of milk and the use of suitable substitutes. If our results at the Phipps Institute are any criterion, common sense methods in utilizing the food at hand will give satisfactory results.

The prevalence of malnutrition in school children is the subject of an interesting article by Maud A. Brown.<sup>74</sup> In one of the schools which she investigated, 41 per cent. of the children were more than 10 per cent. underweight.

Adults often fail to realize that the growing child will consume and really needs more food than the grown person. Benedict and Benedict<sup>75</sup>

<sup>73</sup> Journal of Biological Chemistry, March, 1920.

<sup>74</sup> Journal of the American Medical Association, July 3, 1920.

<sup>75</sup> Boston Medical and Surgical Journal, October 21, 1919.



emphasize this point. In commenting on the energy content of extra food, they point out that analyses of the weights of children point to the fact that every effort should be made to have children somewhat over-rather than underweight. They believe that the common raids of the small child upon the pantry if not of sufficient frequency to upset digestion, are not physiologically unsound. The providing of a small lunch at certain definite times would obviate this. The essential thing to remember is that the active healthy child has usually an extraordinarily good digestion and needs large amounts of food.

The necessity of an efficient nurse in a study of this kind is emphasized. But I agree with Emerson that the securing of a good nurse is much easier than obtaining a physician who will evince the interest in the children and infuse the necessary "pep" to make a class of this kind a success.

VITAMINES. The value of orange-juice as an antiscorbutic has long been recognized. Not only the juice but the rind has also been shown to contain the necessary vitamin which cures or prevents *scurvy*. In addition to its antiscorbutic properties, Osborne and Mendel<sup>76</sup> have shown that both the juice and inner peel of the orange contain the *antineuritic vitamin* (water-soluble B). This finding has been confirmed by Byfield, Daniels and Loughlin.<sup>77</sup> The latter found that if the amount of orange-juice ordinarily used for antiscorbutic purposes (15 c.c.) was increased to 45 c.c. a day in infants whose weight was remaining stationary, they promptly gained, and that this gain did not occur if the food intake was increased. It has previously been shown that if the antineuritic vitamin is removed from the orange by absorption, growth is not stimulated, although the antiscorbutic properties are still retained. It is thus seen that the orange contains two highly valuable food ingredients.

I have already spoken of the difficulty at the present time of securing milk, and the emphasis some have placed on this article of food as a necessary ingredient for stimulating growth. It is interesting to note that Osborne and Mendell<sup>78</sup> point out that relatively large quantities of milk are required to produce the increased intake of food and improved rate of growth which are readily secured by very small quantities of many green vegetables.

During the war, the scarcity and the high prices of oranges led to the investigation of other fruits and vegetables. Among these is the tomato, the value of which as an antiscorbutic was first pointed out by Hess. A study of the food properties of this vegetable by Osborne and Mendell<sup>79</sup> show that it is one of the most valuable of all the foodstuffs as it contains all the now-recognized vitamin properties—the antineuritic (water-soluble B), the antiscorbutic and the fat soluble (the fat-soluble A characteristic of milk fat and egg fat).

Hess<sup>80</sup> again calls attention to the value of the canned tomato as an

<sup>76</sup> Proceedings of the Society of Experimental Biology and Medicine, November, 1919.

<sup>77</sup> American Journal of Diseases of Children, May, 1920.

<sup>78</sup> Journal of Biological Chemistry, April, 1920.

<sup>79</sup> Ibid.

<sup>80</sup> New York State Journal of Medicine, July, 1920.



antiscorbutic for artificially-fed infants. He recommends it in doses of an ounce a day and by substituting it for orange-juice, a great saving is affected.

Mendel<sup>81</sup> states that 0.1 gm. of butter fat fed daily in addition to an otherwise adequate diet suffices to enable rats to grow to adult size before they show symptoms of nutritive decline that are remediable by further addition of the fat-soluble vitamin. He also states that dried tomato as a source of fat-soluble vitamin is even more satisfactory.

It has thus become apparent that fruits and vegetables are of great value over and above the antiscorbutic properties which have always been attributed to them. This is largely due to the fact that they contain the water-soluble antineuritic vitamin which exerts a very potent influence in the stimulation of growth.

In a discussion<sup>82</sup> on the antiscorbutic properties of limes and similar fruits, it was brought out that fresh lemon-juice is far superior to that of the lime, the latter being only one-fourth as strong as the former. This seems to be partly due to the fact that the limes have to be picked and the juice preserved at a certain time in order to get the full value of the juice. If this is not done, scurvy may develop in spite of the lime-juice.

It is also pointed out that limes from the West Indies have been particularly lacking in antiscorbutic properties and are to be avoided if limes are to be used for this purpose.

Osborne and Mendel,<sup>83</sup> in a preliminary study of the vitamin content of the orange, lemon and grapefruit state that it seems doubtful whether the juices of the lemon or grapefruit contain more than traces, if any, of the fat-soluble vitamin. Observations on orange-juice point to some potency in this vitamin.

In a study of the vitamin content in milk, Hart, Steenbock and Ellis<sup>84</sup> found that the amount of the antiscorbutic vitamin was influenced by the season of the year. Summer pasture milk is much richer in this vitamin than dry feed milk or winter-produced milk, involving the use in the ration of corn silage or sugar mangels.

In addition to their vitamin content, the citrus fruits have long had attributed to them a laxative potency. It is to be borne in mind, however, that these fruits also contain more or less indigestible vegetable constituents and it may be that the irritating effect of this material stimulates the gut. In this connection it is interesting to note the observations of Gerstenberger and Champion<sup>85</sup> to the effect that orange-juice is not a laxative but exerts a constipating effect. In their opinion, orange-juice is to be used as an antiscorbutic and not specifically for the relief of constipation. In infants and children who have a tendency toward constipation, the use of orange-juice aggravates, rather than relieves, this condition.

<sup>81</sup> New York State Journal of Medicine, July, 1920.

<sup>82</sup> Journal of the Royal Army Medical Corps, 1919.

<sup>83</sup> Journal of Biological Chemistry, July, 1920.

<sup>84</sup> Ibid.

<sup>85</sup> American Journal of Diseases of Children, August, 1919.

The rôle of the antineuritic vitamin in the artificial feeding of infants has been investigated by Daniels, Byfield and Loughlin.<sup>86</sup> Their conclusions are as follows:

1. The addition of the antineuritic vitamin obtained from wheat embryo to the diet of babies supplied with food furnishing an adequate number of calories stimulated growth.

2. The beneficial influence of adding a specially prepared vegetable soup in sufficient quantity as part diluent in the milk modifications for infants is apparently due to the presence of the antineuritic vitamin contained therein. Both the alcoholic soluble material of the dried soup vegetables and the water extract (soup) stimulated growth.

3. The fact that the artificially-fed infant requires a larger amount of food than the breast-fed infant appears to be due to the relative paucity of diluted cow's milk in the antineuritic vitamin.

4. It is probable that failure to gain in infants and young children is often the result of an insufficient amount of the antineuritic vitamin in the food. The diets of the young, they believe, should be more carefully scrutinized with this in mind.

Two articles on the effect of *vitamin deficiency as a cause of gastro-intestinal disorders* have been contributed by McCarrison.<sup>87</sup> He states that dietaries excessively rich in starch or fat, or broth and at the same time lacking in sufficient vitamin and protein are potent causes of disease, particularly gastro-intestinal disorders. An excess of fat in association with a deficiency of B-vitamin and protein, and a superabundance of starch, is particularly harmful. Certain dietetic deficiencies greatly favor the invasion of the blood and tissues by bacteria; especially is this the case when deficiency of vitamins and protein is associated with an excessive intake of starch. In the monkey, a complete deprivation of B-vitamin, especially if there be also imperfect balance in other essential requisites of the food, will lead to rapid dissolution and death. McCarrison believes that the data obtained from these dietetic experiments may afford some explanation of the cause of that great mass of ill-defined gastro-intestinal disorders and vague ill health which forms so high a proportion of human ailments at the present day.

In his second article, he emphasizes the importance of a study of the dietetic habits in every case of gastro-intestinal disorder as many of these conditions are in some way connected with dietetic deficiency and lack of balance of the food. Among these conditions, he mentions mucous disease of children; celiac disease, intestinal toxemia and gastro-intestinal stasis. These conditions, he states, are readily produced by a diet deficient in vitamins and suitable protein while excessively rich in carbohydrates.

FAT. In a study of *fat metabolism* in infants and young children, Holt, Courtney and Foles<sup>88</sup> found that corn oil and nut butter are valuable foods for children, are exceedingly well borne and are appar-

<sup>86</sup> American Journal of Diseases of Children, December, 1919.

<sup>87</sup> British Medical Journal, February 21, 1920; Ibid., June 19, 1920.

<sup>88</sup> American Journal of Diseases of Children, September, 1919.

ently digested and absorbed with ease. It is their belief that these articles may safely be introduced into the regular diet of children, and that to a considerable degree they may be substituted for the more expensive milk fat, given either as milk or as butter, but that they should never entirely replace the milk fat.

This is exactly in line with our experience at the Phipps Institute in feeding undernourished children of the poorer class who could not afford to buy milk in the quantities they formerly did.

These observers point out, what the dairy adherents fail to make clear, that there is as yet not available the data to determine the amount of *fat-soluble vitamin* required for normal growth and nutrition. Reference has already been made to the value of the tomato in furnishing the fat-soluble vitamin.

Hindhede<sup>89</sup> has contributed an interesting article on the effects of the food restrictions that were imposed on the Danish people as a result of the blockade during the latter years of the war. The plan adopted by the Danish Government consisted of reserving the available cereals, notably rye, wheat, barley, as well as a large proportion of the potatoes grown in Denmark, for the people instead of feeding them to the domestic animals, particularly cattle and hogs. As a result of consuming the vegetable products directly, so many of the hogs were killed that the number was reduced to one-fifth the pre-war stock. As a result, the meat supply, and particularly the fats, were greatly reduced. Fat has always been considered as an absolute essential to the diet and this has assumed increasing importance because of discovery of the fat-soluble vitamin and the rôle it plays in growth and development. Hindhede has shown that individuals have been maintained for many months in good health and vigor on diets of bread, potatoes, vegetables and fruits without any added fat whatever.

In this connection the dietary of the Italians might be considered. Several years ago, in a study made at the Phipps Institute of the dietetic habits of several different nationalities, we found that the Italian's diet was made up of a little more than 75 per cent. carbohydrate. The amount of fat and protein is very small. They eat very freely of the fresh vegetables, particularly tomatoes. The lack of ill effects of the fat-free diet imposed on the Danish people is probably to be explained by the fact that the fat-soluble vitamin contained in milk, butter, eggs and animal fats was supplied by vegetables, particularly the tomato, which Osborne and Mendell have shown to contain all the known vitamin potencies.

**BOTULISM.** During the past year the country has been startled by the frequency of deaths due to botulism. A distressing feature is the fact that in most instances several members of a family or a group of people dining together, have died or become seriously ill as the result of eating food contaminated with the *Bacillus botulinus*. The first reported cases were due to the ripe olive but other articles of food in common use have also been responsible. It is to be noted that,

<sup>89</sup> Journal of the American Medical Association, February 7, 1920.



aside from the ripe olive, the other articles of food have almost invariably been "home-canned." Among these may be mentioned string beans, corn, asparagus, apricots, peas, etc. So far as I know, none of the vegetables put up for sale by commercial houses have been responsible, with one exception. Randell<sup>90</sup> has reported an outbreak of poisoning from the use of commercially canned beets. In this case the beets were eaten directly from the tin container with some vinegar poured over them. Other articles of canned vegetables eaten at the same meal were thoroughly cooked.

Sisco,<sup>91</sup> in reporting the outbreak in New York, states that three of the olives examined were in a turbid, brownish, tinged with red, watery fluid which was very difficult to see through. There was a slight flocculent precipitate in the bottom of the bottle. The olives themselves were lighter in color than ordinary ripe olives, having a tan, buff, almost straw color. They were somewhat spotted, each olive having several distinct black spots in it which stood out sharply from the lighter, general color, possibly areas from which the normal black color had not yet faded. In addition, there were small, whitish flocculent, irregular lichen-like spots giving somewhat the impression of being deposited on the surface, scattered irregularly over each olive. They had also lost the shining luster usually seen in normal ripe olives and were softer than normal. They were not, however, actually mushy. In the case of these olives there was some question as to whether there was a distinct putrefactive odor. Some who examined them believed there was, others were uncertain, and doubted whether it was present, at least sufficiently so to cause suspicion. Seven weeks later the olives showed, in an accentuated form, the defects stated above.

It is interesting to note that the olives described by Sisco were part of a consignment packed by a California Company for a distributing agency in New York and rejected by the latter as "impossible." They were placed in a storehouse, repacked and sold by another company. While many bottles of this consignment were sold, and presumably eaten by others than those reported by Sisco, it is not known whether others were affected or not. Presumably they were not, or only so slightly so as to cause no serious trouble.

*Etiology.* The cause of the poisoning is the *Bacillus botulinus*, of which there are two types, at least so far as their toxin-antitoxin relationships are concerned (Dickson and Howitt). It is apparent that the presence of this organism in a locality leads to contamination of the food. If this is put up in tins or jars and has not been thoroughly sterilized, the bacillus remains intact. It is apparent that in most instances there is no reason to suspect the canned goods, so far as odor or appearance are concerned. In some cases the food has shown, after the poisoning and on closer investigation, to have a slightly putrefactive odor, but this does not seem to have been marked enough to cause the article in question to be rejected. The ripe olive has

<sup>90</sup> Journal of the American Medical Association, July 3, 1920.

<sup>91</sup> Ibid., February 21, 1920; Ibid., March 6, 1920.

attracted the most attention as a "carrier" of the *Bacillus botulinus*. The green olive has, so far, never been implicated. This is to be ascribed to the fact that the ripe olive is subject to little preparation before being put in a container, while the green olive is passed through a number of processes which would apparently eliminate the organism. As already stated, other food articles, such as string beans, asparagus, etc., put up by the housewife have also caused outbreaks of the disease. In the latter instance, as in the use of the ripe olive, inefficient sterilization fails to kill the organism if present. Greenfield<sup>92</sup> stated that the toxin formed by the *Bacillus botulinus* in canned, ripe olives can be destroyed readily by heat. This does not materially affect the flavor of the olives, even when boiled for fifteen minutes. This will also exaggerate the odor of decomposition and tend to discourage eating olives partially spoiled. While the method is simple, it is hardly likely that the desire for ripe olives will induce many people to risk this article of diet.

Outbreaks of botulism have occurred in Detroit, New York, Canton, O., Florence, Arizona, Albany, N. Y., Seattle and several localities in California. To date, there have been about 150 cases.

Aside from its medical interest, botulism is of great economic importance. For example, the widespread fear of ripe olives has led people even to distrust the green olive. The result has been that the olive growers of California have suffered a serious monetary loss. In their dilemma the growers have turned to medical men for aid, and have made a large grant to one of the pathological laboratories in California so that the method of spread and the prevention of this trouble may be studied. I understand that the growers stand ready to appropriate as much money as necessary; and well they might, in view of the financial loss they face if the problem cannot be solved. It is interesting to recall that two similar occurrences in France gave Pasteur two of his greatest scientific triumphs and saved two great national industries from ruin, namely, the grape vineyards of the wine producers, and the silk-worm industry. In view of the number of outbreaks following the use of "home canned" vegetables, it behooves all who put up their own vegetables to be certain that sufficient heat is applied to kill any organism that may be present.

*Symptoms.* Evidences of poisoning develop in from three or four hours to two days after the ingestion of the contaminated food. The symptoms, as a rule, develop gradually, and may at first cause no apprehension. The two dominant features of botulism are difficulty in swallowing and disturbance of speech owing to paralysis of the pharyngeal muscles, and ocular manifestations. In addition, there is marked prostration.

The patient is apt to first complain of some depression and difficulty in expectorating or swallowing. As the disease progresses, the mucus becomes thicker, glairy and more tenacious and cannot be either swallowed or expectorated. The discomfort from this is so great that

<sup>92</sup> Journal of the American Medical Association, March 6, 1920.

the patients attempt to remove it with their fingers or a handkerchief. As the paralysis of the pharyngeal muscles becomes more marked, the speech disturbance increases, and there may be complete aphonia. There may also be a feeling of tightness about the throat and a sensation of choking. In one of Randell's cases, the patient was, until within a few hours of death, able to rise in bed, but owing to paralysis of the cervical muscles had to lift his head about with his hands. Nausea and vomiting occurs frequently. Evidences of intestinal irritation do not occur as in the case of ptomaine poisoning. Dizziness and a staggering gait may often be present.

Among the ocular symptoms may be mentioned, dimness of vision, diplopia, ptosis of the eyelids and occasionally nystagmus. Randell noted in his cases that the pupils were dilated and did not react either to light or accommodation. De Saint-Martin<sup>93</sup> noted in four cases the presence of extreme and persisting congestion of the papilla and retina, with amblyopia. The optic nerve and retina lesions were evident six months later; in addition there was considerable contraction of the visual field for white and even more for other colors, but there was no scotoma or imperfect discrimination of colors. In these cases the asthenia was extremely prolonged after the subsidence of the acute symptoms. De Saint-Martin believes these eye-ground changes may be of service in the diagnosis of botulism during and after the attack.

As a rule, there is some fever; the pulse-rate is not unduly accelerated. The respiratory rate is not much increased, although there is considerable difficulty in breathing. Toward the end of the disease the breathing becomes more difficult; cyanosis appears. Chilliness and profuse sweating are noted in some cases. Sisco states that in the cases observed by him that the mind remains remarkably clear until shortly before death when the patients become drowsy and finally comatose.

*Treatment.* The promotion of free elimination, stimulants, and, if obtainable, the use of antitoxin are the essential features of the treatment of this condition. Owing to the difficulty in swallowing, cathartics cannot, as a rule, be given by mouth. The bowel is best emptied, therefore, by high enemas. Stimulants, such as digitalis, coffee, etc., are also best given per rectum or hypodermically.

At the present time promising results are to be expected from the production of a satisfactory antitoxin. Such an antitoxin has already been used with quite good results but as yet none is available for commercial distribution. Reference to this was made in the December, 1919, issue of *PROGRESSIVE MEDICINE*. Dickson and Howitt<sup>94</sup> have been experimenting along this line. They prepared an antitoxin by injecting goats with several strains of the *Bacillus botulinus* over a period of several months.

At the present time the only known source of supply is that prepared by Graham at the University of Illinois. In the Detroit outbreak, Jennings, Haas and Jennings<sup>95</sup> used the serum in 2 cases. In

<sup>93</sup> Bull. de la Soc. méd. des hôp., January 16, 1920.

<sup>94</sup> Journal of the American Medical Association, March 13, 1920.

<sup>95</sup> Ibid., January 10, 1920.



1 they injected 42 c.c. of the serum intravenously without any apparent effect, in another case they gave two injections of 20 c.c. each and the patient recovered. As the latter was a very mild case, they could not state whether the serum should be credited with the recovery or not. As the result of their experimental studies, Dickson and Howitt conclude that: (1) A true antitoxin may be prepared for the toxin of *Bacillus botulinus*. (2) There are at least two types of the organism which are distinct so far as their toxin-antitoxin relationships are concerned. (3) Experiments show that in the laboratory the antitoxin may protect against the action of the toxin for at least twenty-four hours after the administration of one test-dose of toxin, but that the effectiveness is, to a certain extent at least, dependent on the amount of toxin injected. (4) For therapeutic administration a polyvalent antitoxin should be employed, and it should be given in large amounts and intravenously.

**DIABETES.** The modern treatment of diabetes aims first to get the patient sugar-free either by the Allen method of starvation, or, in very severe cases, with threatening acidosis, by a more or less rapid reduction of the diet. Having gotten the patient sugar-free, the diet is gradually built up until the point of tolerance for carbohydrate and fat is reached. Following the starvation period, it is Allen's plan to use thrice boiled vegetables from which most of the carbohydrate has been removed.

Cambridge<sup>96</sup> has analyzed seventeen of the commonly used vegetables, often boiling them once, twice or three times. The amount of boiling to remove all the carbohydrate varied with different vegetables. Two boilings would remove all the carbohydrate from celery, rhubarb and spinach, while with white turnips and carrots three boilings were sufficient. In the case of other vegetables tested, even after three boilings, there was left from 0.1 to 1 per cent. of carbohydrate.

In carrying out the treatment of diabetes, the use of these repeatedly boiled vegetables is sometimes difficult because the patients find them so unpalatable. The removal of carbohydrate removes more or less completely the flavor, although this may be overcome, to some extent, by making a vegetable purée with clear broth or other flavoring substances. Cambridge, acting on the suggestion that the carbohydrate might be extracted at a temperature considerably below the boiling-point and without so much interference with the flavor, found that this could be done.

A slight modification of the Allen method is advocated by Langdon Brown<sup>97</sup> as being somewhat preferable, although the principle is essentially the same.

Brown begins the treatment: (1) With two hunger days during which the patient is allowed tea and coffee as usual and 500 c.c. of bovril and broth made without vegetables and divided into two portions. Water or lemonade, sweetened with saccharin, can be taken freely. (2) Two vegetable and egg days. *Breakfast:* Two scrambled eggs, with

<sup>96</sup> *Lancet*, December 27, 1919.

<sup>97</sup> *Practitioner*, August, 1919.

tea or coffee; 2 ounces (50 gms.) of lettuce, watercress or tomato. *Lunch:* Eight ounces of bovril or broth; one poached egg on spinach and green vegetable with  $1\frac{1}{2}$  ounce of butter. The total amount of the vegetables for the meal to be 6 or 8 ounces. *Tea:* Tea or coffee, lettuce, watercress or tomato—2 ounces (50 gms.). *Dinner:* Eight ounces of bovril or broth, two eggs, cooked as desired, *e. g.*, as a savory omelet; 6 to 8 ounces of green vegetables with  $1\frac{1}{2}$  ounces of butter. Water or lemonade as desired. This diet has a caloric value of 1170 and a carbohydrate intake of about 10 gm. (3) *Ladder diet:* After two vegetables and egg days add 50 grams of meat or 100 grams of fish. This increases the caloric value to about 1300. Two days later add 50 grams of bacon at breakfast and omit one egg. Add another 10 grams of butter to the vegetables. The caloric value is now 1595. Two days later add 50 grams of sardines at lunch, and omit one egg or if the fish has previously been given, omit this and add 100 grams of meat. The caloric value is now 1635. Two days later add 50 grams of ham and omit another egg. The caloric value is now 1795. The quantities of ham and sardines may be doubled if the patient is hungry and the degree of acetonuria is slight. This brings the caloric value up to 2145. Rest in bed is advisable, at any rate until the caloric intake reaches 2000.

The dietary increase just given takes twelve days to reach the top. If the patient is then free from sugar add another 100 c.c. of milk (=4 grams of carbohydrate) or 10 grams of bread (=6 grams carbohydrate in war bread, and 5 grams in ordinary bread). Increase this amount daily until the carbohydrate tolerance is reached. If the patient is not sugar-free when the top of the "ladder" is reached, start in again and repeat the whole process.

As a rule, Brown gives two egg and vegetable days once in two weeks and two hunger days followed by two egg and vegetable days once a month. In each case the patient returns to his "tolerance" diet immediately after these days.

Allen states that diabetics die from three main causes: Coma, tuberculosis and gangrene. The association of *tuberculosis* and diabetes is relatively common, and when it occurs forms one of the worst combinations possible! Up until within the past few years, it was usually looked upon as hopeless. The great majority of these cases were treated, if any treatment at all was seriously considered, from the point of view of the tuberculosis. The diabetes was ignored. The result was that the diabetes tended to grow worse and, as a consequence of the malnutrition it caused, the tuberculosis also grew worse.

Several years ago, at a meeting of the Association of American Physicians, I heard Allen report examples of diabetes complicated with carbuncle. In spite of the deplorable condition of these patients, much the same treatment, namely, preliminary starvation followed by a low caloric diet, was followed in these patients as in uncomplicated cases. His contention was that no improvement could be hoped for so far as the carbuncle was concerned unless the diabetes was controlled. If this could not be done, the complication would inevitably kill the patient.



In view of the hopeless outlook in cases of associated tuberculosis and diabetes, it occurred to me that the same treatment should be followed in these cases, namely, to aim at controlling the diabetes and to some extent ignore the tuberculosis; in other words, reverse the prevailing practice. Shortly afterward this plan was put in operation at the Phipps Institute and the White Haven Sanatorium. It cannot be denied that in the first two or three cases it took considerable courage to carry the treatment out. This can readily be understood when it is recalled that the two essential features in the treatment of tuberculosis are rest and hyperalimentation, while in diabetes two important features are exercise and a marked restriction of food, much of the latter being especially desirable in tuberculous cases.

To see a case of active tuberculosis lose from ten to twenty pounds when already under weight is certainly not encouraging. While this is going on, however, and providing the case is not hopeless, the fever grows less day by day, the cough and expectoration diminish and the general well-being of the patient improves. At the same time, the patient becomes sugar-free. If the patient can be gotten sugar-free, all, or most all, of the weight lost during the starvation period and period of low diet is regained. This is possible, of course, only when the two diseases are relatively mild. If the tuberculosis is of the severe type or the diabetes is severe, and in either case apt to cause a fatal issue if uncomplicated, nothing is to be hoped for.

A few months ago I saw the relative of a physician who had extensive infiltration of the right upper lobe, fever of 100° F. every afternoon, severe cough and expectoration and some loss of weight. In addition, she had a moderately severe diabetes. She was treated with the Allen plan and in two months was free from the symptoms of tuberculosis.

The results of my experience with this combination were reported by Montgomery, Funk and myself in the *American Review of Tuberculosis* two years ago.

Recently, an article on this subject has been published by Janney and Newell.<sup>93</sup> Their report deals with 16 cases. They state that data available indicates that the untreated diabetic is more likely to develop pulmonary tuberculosis than when maintained sugar-free by modern dietetic methods.

In a series of 16 diabetic cases complicated by pulmonary tuberculosis showing activity, 12 patients definitely improved during a course of institutional treatment; diabetic symptoms disappeared in all but 2 cases, observed but a short interval. Tuberculous symptoms improved in the majority of cases.

The principles of treatment recommended are: The judicious employment of sufficient undernutrition, combined with rest, to maintain the patient sugar-free and control the tuberculosis. Fasting is unnecessary to obtain good results. Ill-advised fasting, in the opinion of Janney and Newell, may lead to a fatal outcome. Rest is at least

<sup>93</sup> Journal of the American Medical Association, July 17, 1920.



as important as in the treatment of uncomplicated pulmonary tuberculosis.

In regard to fasting, I can only say that in the moderately severe cases it can be followed with safety. Whether one shall institute the treatment with a fast period or gradually reduce the carbohydrate intake will depend on the severity of the two diseases and also whether there is an impending acidosis. One other caution, and that is in regard to the use of fats. Fat should be used as sparingly as carbohydrate. To try and increase the caloric intake by pushing fats is a mistake.

Densten<sup>99</sup> cautions against too strenuously treating a diabetic passing less than 2 per cent. of sugar. It is also well to remember that there are individuals who pass sugar one day and not another. He strongly advocates the use of *alcohol* in some form for the diabetic who continues to pass over 2 per cent. of sugar or continues to lose weight.

The treatment of experimental diabetes in dogs from a nutritive standpoint is summarized by Allen<sup>100</sup> as follows: In most cases life, strength and assimilation can be preserved for a much longer time by a degree of undernutrition suited to the severity of the diabetes and accomplished by limitation of fat in the diet. The permanence of such control is supported by the unimpaired or rising assimilation in experiments of one to one and three-fourths duration, but still longer observations would be desirable. Diabetes of great severity is controllable only by correspondingly radical undernutrition. In still more severe cases, glycosuria can be abolished only by a degree of undernutrition which entails final death from inanition.

HEART DISEASE. Attention to the diet in the management of cases of *cardiac insufficiency* is emphasized by Rubow.<sup>101</sup> He considers that the most important things are the calory content and the salt and water content of the food. Restricting the diet along these lines, supplemented with rest, is often sufficient to relieve dropsy. In the severer cases cardiac stimulants are also used.

The *Karell treatment* is best adapted for these cases. This treatment consists of keeping the patient at absolute rest in bed and allowing nothing in the way of food but 800 grams of milk in twenty-four hours. The specific action on the edema from the Karell treatment is evidently due to the small intake of water. Furthermore, the heart is taxed less and the removal of salt increases osmotic interchanges. This results in an increased diuresis and the rapid elimination of the salt retained in the tissues. Elimination is also promoted through the skin by sweating procedures.

In some cases, the edema disappears in the first day or so without a material increase of the diuresis; later there may be a more less increase of the diuresis. This is probably to be explained by lessened metabolic activity and the decreased work of the heart. It is also possible, in

<sup>99</sup> New York Medical Journal, October 11, 1919.

<sup>100</sup> Journal of Experimental Medicine, May, 1920.

<sup>101</sup> Hospitalstidende, April 13, 1919. Abstract, Journal of the American Medical Association, October 4, 1919.

Rubrow's opinion, that the lesser volume of the blood coöperates in relieving the insufficiency of the heart functioning.

Rubrow states that another advantage of the Karell course is that the lessened intake of salt reduces the thirst.

In treating the case after the Karell course, the diet must be water-poor and salt-poor, and the caloric intake reduced to the actual needs of the patient. The use of digitalis, absolute rest and the Karell treatment for a few days every month may control the cardiac condition for years.

Krehl<sup>102</sup> also emphasizes the importance of rest and a milk diet. He deplores the neglect of these measures and the indiscriminate use of digitalis in the management of cardiac insufficiency.

Isenschmid<sup>103</sup> states that the lack of milk in certain countries during the war, prevented the use of the Karell treatment of heart disease. This led to certain substitute measures which, he says, were even more efficacious than the original method. Thus instead of milk, 1 liter of water or fruit juice is allowed for the beverage, and 1 kgm. of potato, cooked without salt, is given during the day in five portions. In place of the potato, banana may be used. As the Karell treatment and its substitutes are poor in salt and given in small quantities, the absence of metabolic waste and the restricted amount of fluid make very small demands on the digestive system and the kidneys. Isenschmid also found that restriction of albumen and of fluid and of salt is more effectual in the edema of heart disease than the restriction of salt alone. He states that the edema following dysentery and other protracted wasting infectious diseases is usually ascribed to weakness of the heart, but, in his opinion, it is more probable that it is of the starvation edema type. Other known factors may be concerned, but, to date, a diet conforming to the above principles seems to offer the best prospects for the cure of edema.

NEPHRITIS. Whether true or not it has become traditional to restrict the use of protein food, particularly red meat, in the treatment of nephritis. As the result of repeated observations, MacLean and Russell<sup>104</sup> are of the opinion that, in general, patients suffering from interstitial nephritis of moderate severity should be allowed a fairly liberal diet in which protein need not necessarily be cut down to any great extent. In severe cases, it is probably best to depend chiefly on carbohydrate food.

In cases of parenchymatous nephritis, in which there is no retention of nitrogenous products in the blood, there does not seem to be any theoretical objection to giving protein or urea. In the opinion of MacLean and Russell there is no proof that protein acts detrimentally, even in advanced interstitial nephritis, but, on general principles, it is probably best to limit the intake of protein in patients showing a marked nitrogen retention. Mild cases of interstitial nephritis do not seem to be especially benefited by very strict dietetic restrictions.

<sup>102</sup> *Deutsch. Arch. f. klin. Med.*, January 27, 1920.

<sup>103</sup> *Schweizerische med. Wchnschr.*, May 6, 1920.

<sup>104</sup> *Lancet*, June 19, 1920.



PELLAGRA. This disease continues to be the subject of discussion as to its etiology. By many, probably most observers, pellagra is regarded definitely as a food deficiency disease. There are others, however, who, although in the minority, do not accept this view. Several years ago, in an intensive survey, the inhabitants of a small town in the South, among whom pellagra had existed off and on for years, were thoroughly studied. The investigators came to the conclusion that factors other than food played an important part, notably unhygienic surroundings. Visivalingam,<sup>105</sup> after careful study, is one of those who does not believe that a faulty diet alone can cause pellagra. If diet is the sole factor, then the affected individual should improve and there should be no recurrence when he is removed to a hospital and placed on a liberal diet; but this is not so. In his opinion there is needed a superadded infection. The habits of the people, a poor dietary, bad hygienic surroundings, gastro-intestinal infections, chronic fibrosis seen in the organs drained by the portal circulation, and many other minor factors, favor the view that the infection must be through the intestinal canal. He points out that the seasonal recurrence of symptoms in patients removed from their surroundings and placed in a hospital with an adequate diet for considerable periods of time, would point to the presence of an endotoxin resulting from the evolution of some organism or more probably the establishment of a vicious circle brought about by profound metabolic changes.

Among predisposing causes, Visivalingam mentions dysentery, ankylostomiasis, malaria and scurvy. He found evidences of one or the other of these conditions present in at least 60 per cent. of the cases seen by him.

RICKETS. The essential and central feature of rickets, in Pritchard's<sup>106</sup> opinion, is the want of calcification or mineralization of developing bone and this in turn is due to the existence of requirements for calcium which for the time being are more urgent than of developing bone. He holds the view that practically all varieties of malnutrition occurring during infancy and early childhood tend to terminate in rickets, provided they are sufficiently severe or long enough continued. They should not, however, be regarded as evidence of rickets, unless they are actually accompanied by the typical changes in bone which are characteristic of the disease.

Pritchard believes that all chronic conditions of malnutrition, of whatever kind or from whatever cause, finally terminate in an acidosis, and that all claims on alkaline basis arising in connection with the neutralization of this acidosis must be satisfied before those of developing bone are attended to.

Losser<sup>107</sup> believes that tardy rickets is the link between rickets and *osteomalacia*. The cases observed by him were between twelve and twenty years of age and in some of the cases the rickets had existed since early childhood. He believes that the so-called growing pains,

<sup>105</sup> Journal of Tropical Medicine and Hygiene, February 16, 1920.

<sup>106</sup> New York Medical Journal, December 6, 1919.

<sup>107</sup> Correspondenz-Blatt f. Schweizer Aerzte, July 17, 1919.



rheumatic pains in young adults are manifestations of tardy rickets, and this he affirms is the same thing as osteomalacia. The condition is relieved by the use of phosphorus, 2 or 3 mg. daily and kept up for months.

Bohme<sup>108</sup> also comments on the similarity of rickets and osteomalacic affections. He has applied the treatment in rickets to osteomalacia, namely, a highly nutritious diet that is sufficiently varied, prevention of unnecessary weight-bearing by the bones and the administration of cod-liver oil with phosphorus.

The studies of Hess and Unger and others indicate very clearly that rickets is a food-deficiency disease and can be prevented or may be cured by proper diet. Mellanby<sup>109</sup> states that evidence has accumulated which indicates that an excess of carbohydrates increases the tendency to rickets, that proteins have an antagonistic action to the development of rickets. Casein seems to have the same effect. If the antirachitic effect of protein is established, this explains why milk is a better preventive of rickets than a corresponding amount of butter. It has also been shown that the antirachitic factor is fairly high in some vegetable fats, such as, for instance, peanut, cottonseed and cocoanut oils, and is present only to a small extent in palm kernel, linseed and babassu oils. Mellanby quotes the results of a survey made in an English city of Jewish and Gentile children in which it was shown that the former were much better developed. The Jewish families used a great deal of oil in cooking. Oil, butter, milk, fish, eggs, meat and vegetables were freely used. He states that a similar condition exists in one of the islands of the Hebrides.

Active rickets is rare after the second year of infancy. This is about the time the milk is cut down.

**SCURVY.** One of the oldest beliefs in regard to food deficiency is that scurvy is definitely related to dietetic errors. Most commonly seen in expeditions extending over long periods of time and with a lack of fresh vegetables or fruit juices it has also been known for some time that scurvy is far more frequent among infants than is usually believed. Curiously enough, the children of the well-to-do furnish relatively numerous examples of the disease. Last winter there was admitted to the wards of the University Hospital a man with a most severe case of scurvy. He had lived in Philadelphia for years. An investigation of his dietetic habits revealed the fact that he had been subsisting for months on a diet of beans, pork and bread, and, so far as could be learned, he had taken no fresh meat, fresh vegetables or fruits of any kind. The use of orange-juice caused the almost miraculous disappearance of the signs and symptoms of scurvy.

This traditional view of scurvy has been combated by several observers who have attempted to show that the disease was not a food deficiency disease but was caused by other factors. Thus, McCollum attempted, unsuccessfully, to show that it was caused by chronic constipation, and Coplous, Jackson and others, that the disease was

<sup>108</sup> Deutsch. med. Wchnschr., October 16, 1919.

<sup>109</sup> Lancet, April 17, 1920.

of bacterial origin. The latter hypothesis has been investigated by Givens and Hoffmann.<sup>110</sup> These observers made bacteriologic examinations of the blood and tissues of scorbutic animals. No matter what the character of the diet was, they found the blood to be sterile. The enlarged front joints of guinea-pigs developing scurvy on oats alone were sterile, and this was true in nearly all the guinea-pigs developing scurvy on other special diets. While in a few instances staphylococci or diplococci were isolated, these organisms could not be made to produce scurvy when inoculated into healthy guinea-pigs. Givens and Hoffmann also found that the intestinal flora showed no differences in scorbutic and non-scorbutic animals which would explain the cause of scurvy. The antiscorbutic properties of raw beef have been studied by Dutcher, Pierson and Biester.<sup>111</sup> They produced scurvy in guinea-pigs. When water extracts of raw, lean beef were fed representing 5, 10, 15 and 20 grams of raw beef, they could note no difference in the time of onset of the scurvy or in the length of life of the animals. On the other hand, *orange-juice* added to the basal diet prevented scurvy, both with and without meat extract. The excellent condition of the animals on the orange-juice-beef-extract diet proved conclusively; in their opinion, that the poor condition and death of the animals was due to the absence of the antiscorbutic *vitamin* rather than to any deleterious property of the beef extract.

Comrie<sup>112</sup> saw a good deal of scurvy in the Russian hospitals. The diet consisted of flour or biscuit, rice, oatmeal, peas or beans, frozen or tinned meat or salt herring, pork, tea, sugar, salt, preserved lime-juice (see vitamins, paragraph on lime-juice). Meat and vegetables were all boiled for three hours. On the average, a man developed scurvy on this diet in about four and a half months. That which produced the most prompt response was based on sour milk.

For additional facts regarding the rôle of orange-juice in the prevention of scurvy, see the section on *vitamins*.

**TUBERCULOSIS.** There is no disease which is more subject to dietary vagaries than pulmonary tuberculosis. Some insist that unless certain articles of food are given or withheld no success can be obtained. The truth of the matter is that one does not need to practice dietary fads in order to treat this disease. All that one need remember is that the patient should have three meals a day of ordinary mixed diet. If considerably under weight, the three meals may be reinforced by one or two quarts of milk daily. It is not necessary to avoid vegetables which grow under the ground; to use an excess of red meats; to use a large number of eggs; or to use carbohydrate food sparingly. It has been my experience that the patient who can eat three substantial meals and assimilate his food will probably recover, providing his disease is not too extensive. On the other hand, the patient who has a "finicky" appetite, and who suffers from digestive disturbances, rarely recovers no matter how slight the pulmonary trouble is when first seen.

<sup>110</sup> Journal of Biological Chemistry, March, 1920.

<sup>111</sup> Ibid., January, 1920.

<sup>112</sup> Edinburgh Medical Journal, April, 1920.



Furthermore, I have never seen the latter group lifted out of their trouble by having recourse to invalid foods or any of the dietetic fads. They may be temporarily relieved, but the effect is only transient. In the advanced and hopeless case I generally follow the rule of allowing them to eat what they want and as much or as little as they desire.

Clarke<sup>113</sup> states, in regard to forced feeding, that it is quite impossible to push the nourishment for months or years as is done for the acutely sick during a few days. It is essential to make the eating the most attractive feature of the cure.

**VOMITING OF PREGNANCY.** The use of carbohydrates in treating the toxemias of early pregnancy is advocated by Titus, Hoffmann and Givens.<sup>114</sup> They believe that a deficiency in carbohydrates has an important bearing on the origin of toxemia of pregnancy. This is due to two causes: (1) A relative deficiency due to an unexpected demand for glycogen on the part of the fetus and the uterus; and (2) an actual deficiency, augmented in the presence of nausea and vomiting, from lessened carbohydrate intake.

Mild cases of nausea and vomiting may be controlled by so regulating the diet that there is a preponderance of carbohydrates, and an avoidance of more than short intervals of fasting by the taking of food more frequently than under ordinary circumstances. This increased carbohydrate intake should be augmented by giving the patient from 8 to 16 ounces of 10 per cent. glucose and 2 per cent. sodium bicarbonate solution daily by mouth. This may be given in 1- or 2-ounce doses.

More severe cases require more rapid attention. After an initial period of rest, gastric lavage and the introduction of saline cathartics through the stomach-tube, small amounts of liquid food are allowed alternately with from 1 to 2 ounces of the glucose and soda solution, described above, every two hours. By mouth or by bowel, it should be possible to give the patient a quart of this solution daily.

In the seriously toxic patients, the treatment is pushed even more vigorously, with the addition of intravenous injections of from 15 to 25 grams of glucose in from 250 to 300 c.c. of water. This is given from one to three or more times daily, according to the needs and response of the patient.

Occasionally, an injection of *arsphenamin* is followed by serious symptoms of intoxication which may terminate fatally. In a number of these cases the symptoms resemble those of *acute yellow atrophy of the liver*. Baily and McKay<sup>115</sup> believe that this condition may be aggravated by a high nitrogenous diet. They advise a diet low in fat and protein and rich in *carbohydrates*. This diet should precede the arsenical treatment for several days and be continued throughout the course. The effect of an increase in protein and exercise might be controlled by the estimation of urea in the blood.

**Digitalis.** There can be no doubt but that in the minds of many practitioners any disturbances of the cardiac function calls for the

<sup>113</sup> Boston Medical and Surgical Journal, August 28, 1919.

<sup>114</sup> Journal of the American Medical Association, March 20, 1920.

<sup>115</sup> Archives of Internal Medicine, June, 1920.



administration of digitalis. Krehl<sup>116</sup> states that in his experience it is rare to meet with a case of heart disease of any kind that has not been given digitalis, without any clear idea as to whether the drug was indicated or not. He emphasizes the importance of rest in bed and a milk diet, and points out that these two measures alone will often be all that is necessary. This applies to valvular diseases of all kinds, syphilitic myopathies, cardiac insufficiency associated with chronic nephritis, a rapid or slow pulse or one permanently irregular. The diet should be restricted to from 1 to 1½ liters of milk in twenty-four hours. Such treatment has a most beneficial action on the edema and in restoring the functional capacity of the heart. In his experience, the outlook is more favorable the greater the rise in the specific gravity of the urine as diuresis is increased.

Krehl recognizes the value of digitalis but believes that it is often needlessly used and too often the patient is saturated with the drug.

According to Hare,<sup>117</sup> cardiac cases may be separated into three groups: (1) Auricular fibrillation in which digitalis does great good; (2) cases of rapid heart action, which may be regular or irregular, in which digitalis fails to do good because the condition of the heart muscle is such that it is beyond the influence of the drug; and (3) a large group of cases in which digitalis proves to be as useful as morphin is in the relief of pain.

Sutherland<sup>118</sup> has studied the effects of digitalis in children under fourteen years of age suffering from *acute or subacute rheumatic fever* and who presented a persistently accelerated heart-rate. As has been frequently pointed out, the myocardium in all of the acute infections is often poisoned, and, as a result of this toxemia, the heart muscle cannot respond to the effect of the drug. If, however, there is a sufficiency of sound contractile tissue present in the ventricle, digitalis may exert a most beneficial influence.

In view of the fact that Withering, who introduced the use of digitalis, directed that the drug be given in full dosage, in order to secure the full effects as soon as possible, it is interesting to note that students of cardiac disease are now advocating unusually large doses of the drug not repeated or only at long intervals. Just why the profession failed to follow Withering's instructions, and for years resorted to small doses frequently repeated for days or weeks, is not clear.

Robinson,<sup>119</sup> in an excellent contribution on the effects of a single large dose of digitalis, states that:

"It is this rapid and uniform rate of action of the drug when administered in large single doses, which especially commends the use of digitalis in this manner therapeutically. It is felt that further studies are required before such large doses as were given should be recommended for general use, especially when patients are not under constant observation in hospitals. But the method has been sufficiently tried

<sup>116</sup> Deutsche Archiv. f. Klinische Medizin, January 27, 1920.

<sup>117</sup> Therapeutic Gazette, 1920.

<sup>118</sup> Quarterly Journal of Medicine, 1919.

<sup>119</sup> American Journal of the Medical Sciences, January, 1920.

so that it seems entirely justified whenever rapid digitalis action is strongly indicated, and our experience leads us to believe that it is a much safer method of obtaining rapid digitalis action than the intravenous administration of digitalis bodies, especially strophanthin. Nearly all the cases reported in this series showed very striking clinical improvement within a few hours after the administration of the single large doses of the tincture of digitalis.

"A series of 26 cases of *auricular fibrillation* or flutter is reported, to which large single doses of the tincture of digitalis were administered by mouth. The drug used was standardized, and was usually given in doses ranging from 15 to 25 c.c.

"The study of these cases demonstrates that such doses of digitalis affect the heart of cases of auricular fibrillation or flutter at a relatively constant time after administration, in from two to five hours, indicating that the drug is absorbed from the alimentary tract at a fairly rapid and uniform rate. The series of cases also demonstrates that the maximum effect on the heart is usually obtained in about twenty-four hours, and generally continues to be effectual for from four to fifteen days, or on an average of nearly ten days."

Another article on this subject is contributed by Kay and Tufts.<sup>120</sup> They found large doses most effective in cases of auricular fibrillation associated with a rapid ventricular rate and a marked pulse deficit; also in cases of chronic arterial hypertension with broken compensation. Their method is to give from 20 to 28 c.c. (f3v-vij) of a standardized tincture of digitalis within twenty-four to thirty-six hours. Of this amount, 12 to 16 c.c. (f3iij-iv) are given on the afternoon of admission, and 4 c.c. (f3j) after each of the three meals on the following day. The administration is then stopped and not resumed until clinical or electro-cardiographic observations showed a decline in the effect of the drug. This usually occurred after three to five days. The drug is then resumed in doses of 1 to 2 c.c. three times a day.

Kay and Tufts state that one of the most important things to know before administering these large doses is whether the patient has been taking the drug. If this is the case, an unknown quantity may have accumulated in the body, and under such circumstances the rapid administration of a full dose may produce toxic effects. Under these circumstances, death has followed an intravenous injection of strophanthin. Other conditions which necessitate caution in the administration of large doses are a delayed conduction time between the auricular and ventricular systoles, partial heart block and numerous extrasystoles.

Eggleston<sup>121</sup> states that the appearance of one or more of the following criteria of adequate digitalization, or of minor *digitalis intoxication*, indicates the cessation of further administration, either permanently or temporarily: (1) Nausea or vomiting (except when due to splanchnic congestion and present before treatment is begun); (2) fall of heart-rate (not pulse-rate) to, or below, 60 a minute; (3) appearance of fre-

<sup>120</sup> California State Journal of Medicine, September, 1919.

<sup>121</sup> Journal of the American Medical Association, March 13, 1920.



quent premature contractions; of definite heart-block; or marked phasic arrhythmia, or of coupled rhythm.

The use of a standardized dried aqueous extract of digitalis is reported by West and Pratt.<sup>122</sup> They have employed it in 54 patients. This extract is a fine brown powder which is quite deliquescent, but with care can be kept perfectly dry. The powder is most conveniently dispensed in capsules of 0.1 gm. each. The capsules protect the patient from the bitter digitalis taste, and also aid in protecting the powder from moisture. The oldest sample has maintained its activity for a year.

In practice, in order to avoid nausea that occasionally follows large doses of digitalis, West and Pratt state that it is well to give at the first administration, if the patient has had not digitalis within two weeks, 0.4 gram less than the calculated dose. If, in twenty-four hours, satisfactory results have not been obtained, the remainder can be given. Another method of value is to give at the first administration from 0.4 to 0.6 gram less than the calculated dose, and then after twenty-four hours to give 0.2 gram every six hours until indications for discontinuing the drug are seen. The average dose is 30 mg. per kilogram of body weight.

Hatcher<sup>123</sup> calls attention to the imperative need of a digitalis preparation which will be absorbed from the gastro-intestinal tract with greater uniformity than are the tinctures and other preparations now in use. In addition, there is a need for a preparation of digitalis which can be used intramuscularly or intravenously. In regard to the latter, Hatcher states that the requirements are that: It must be soluble in water, or at least in a weakly alcoholic menstruum; it must be of unusual activity; it must exert a minimum of undesired side reactions; it must not deteriorate rapidly; and it must not irritate the veins or tissues into which it is injected. From studies so far made, he believes that a chloroform-soluble substance meets the requirements for rapid absorption from the gastro-intestinal tract and for use by injection, although the latter is rarely indicated. Eggleston<sup>124</sup> points out that many tinctures are poorly absorbed and may require from four to nine times the average dose without producing a therapeutic effect. On the other hand, the chloroform-soluble extract is absorbed with marked uniformity, and as rapidly as the best tincture. For oral administration, Eggleston states that while the chloroform-soluble extract is not superior to a high-grade tincture, it is far superior to tinctures which are derived from a variety of sources, the absorption of which shows marked differences when the individual specimens are compared. Scott (quoted by Eggleston) employed the chloroform-soluble extract in 8 cases carefully controlled. He states that digitalis action occurred in from one to two hours after 10 c.c. (single dose) by mouth. A definite and striking effect could be confidently looked for in from eight to ten hours.

<sup>122</sup> Journal of the American Medical Association, July 10, 1920.

<sup>123</sup> Ibid., August 14, 1920.

<sup>124</sup> Ibid.



In regard to the unusually full doses which are now being advocated, it is to be borne in mind that the great majority of the observations have been made in hospitals fully equipped with the modern instruments of studying the action of the heart. Controlled in this way, there seems to be no danger. Additional work may show conclusively that the damage is slight and that the drug may be used in large doses by the general practitioner who cannot avail himself of these safeguards.

In addition to its effect on the heart, it is generally recognized that digitalis possesses distinct *diuretic properties*. Jarisch<sup>125</sup> has reported 2 cases in which digitalis exerted an inhibitive action on diuresis when given in full therapeutic doses, but increased this action when given in small dose. He reports two cases of syphilitic aortitis associated with incompetence of the aortic valves. He believes that, owing to the increased excitability of the bloodvessels of the kidney, the threshold for both the vasoconstricting and vasodilating effect of digitalis was reduced. As both patients had evidences of an early contracted kidney, the conclusion may perhaps be drawn that overexcitability of the bloodvessels of the kidney is characteristic of contracted kidney in the incipient stage.

Jarisch believes that full doses of digitalis should be administered with caution in heart patients if the low specific gravity of the urine points to renal sclerosis.

Until more refined methods of studying the arterial tension were introduced, it was the current teaching that digitalis was contraindicated in cases of hypertension as the drug was supposed to raise the pressure. The generally accepted belief now is that the main effect of digitalis is expended in affecting the rhythm of the heart. Its action on irregular hearts, especially auricular fibrillation, is more marked than on regular hearts, although it shows the latter to some extent. While it is true that the blood-pressure is raised by its use in auricular fibrillation, this is a secondary effect due to the improved cardiac action.

Moschcowitz,<sup>126</sup> in referring to these facts, states that much of the former timidity as regards the employment of digitalis in hypertension cases has disappeared, especially in those cases of hypertension with symptoms of decompensation. He points out, however, that the value of digitalis in compensated cases of *hypertension* is not yet appreciated. He has found that the drug is of benefit in these cases although it is not clear as to how this occurs. For example, a patient complains of slight shortness of breath on exertion, pains (often anginoid) about the precordium, and headache or vertigo. An increased blood-pressure is found, the pulse-rate only moderately rapid (80 to 90) and perfectly regular; the urine is lessened in amount and contains albumin and casts. If such a patient is given full doses of digitalis, the symptoms disappear, the quantity of urine increases and the albumin decreases. On the other hand, the systolic pressure declines only slightly and the diastolic pressure somewhat more. The pulse-rate, however, drops from 4 to

<sup>125</sup> Berl. klin. Wehnschr., December 29, 1920.

<sup>126</sup> American Journal of the Medical Sciences, April, 1920.

6 beats per minute and to perhaps 10 or 20, depending on the original rate. If the pulse-rate is kept at this reduced level, the patient will remain well and the objective signs (blood-pressure and urine changes) will remain constant.

Digitalis is not to be used in hypertension cases with a pulse-rate around 60 but may be used if the rate is 74 to 80. Moschowitz states that the use of digitalis in hypertension cases requires careful individualization, but, if these cases are studied along the lines indicated, it will be distinctly worth while.

**Emetin.** MacAdam<sup>127</sup> reports 80 cases of *Endameba dysenterica* treated with emetin hydrochlorid. He administered 18 grains over a period of twelve days. Each day 1 grain was given hypodermically and  $\frac{1}{2}$  grain by mouth. In those suffering from primary dysentery or acute relapses, the entameba disappeared, on the average, in one and one-half days, while the average period of persistence of infection in cyst carriers two and a half days. The symptoms in the acute cases also disappeared rapidly, the average duration being eighteen days.

Of the 80 cases, 18 showed signs of persistent infection during the laboratory examinations; 11 of the relapses occurred among 36 chronic dysenteries. Thirteen of the 18 relapses occurred within four weeks of the completion of treatment. There was no difference between the time of relapse of acute cases and of cyst carriers.

In the management of the *hepatitis associated with amebic dysentery*, Gunn and Savage<sup>128</sup> recommend the administration of 1 grain of emetin for twelve successive days and to follow this with 3 grains of emetin and bismuth iodid for fourteen days.

In very severe cases, where a rapid action of the drug is needed to avert a fatal issue, they recommend giving 1 grain of emetin hypodermically in the morning and 2 or 3 grains of emetin and bismuth iodide by mouth at night. Acute cases which relapse, with symptoms of dysentery, might also be treated with the last-mentioned course.

Carriers which relapse after treatment should be discharged if they have no symptoms. They should be informed that while they are in no danger themselves they are a danger to others. Such individuals, as is the case with typhoid carriers, should not be allowed to handle or prepare food, and should be instructed about the spread of dysentery from the feces.

Pontano,<sup>129</sup> from an experience with 10 cases of liver involvement in *Entameba dysenterica*, believes that emetin therapy is effective even when a *liver abscess* has formed. He injects the emetin intramuscularly daily for three days in doses of from 0.09 to 0.15 grams; two courses are given the first month, and then one a month for eight or nine months. He gives a mild purge before each course, and sometimes gives a decoction of ipecacuanha by rectum. The dysentery may become active at first, but this should not modify the treatment, although the pulse and respiration must be watched for signs of intol-

<sup>127</sup> Indian Journal of Medical Research, January, 1920.

<sup>128</sup> Journal of the Royal Army Medical Corps, November, 1919.

<sup>129</sup> Policlinico, June 7-14, 1920.

erance. Pontano states that the emetin arrests the necrotic process and the abscess contents gradually dry up. If, however, a true abscess, with pus, develops, surgical intervention is necessary.

In addition to its use in dysentery, emetin has been recommended in the treatment of a variety of other conditions, although without much success. LeClerc,<sup>130</sup> for example, has employed emetin in the treatment of *bronchial conditions* simulating asthma. In 2 cases he injected from 0.02 to 0.04 gram daily for five days, suspended the treatment for from five to ten days, and then repeated the injections. The condition he describes is probably a form of chronic bronchitis characterized by attacks of dyspnea somewhat resembling asthma. Such cases are usually due to a bacterial infection and in my experience best treated with an autogenous vaccine. I fail to see how emetin could be of service.

**Eserin.** This drug has been recommended for the relief of tympanites although its action under these circumstances is extremely variable. Montier<sup>131</sup> recommends eserine (physostigmin) in the treatment of sympathetic abdominal pain independent of any organic lesion in the stomach or intestines. Pain of this type is most commonly encountered in individuals suffering from neurasthenia, inanition and ptoses. It may also be encountered in colitis, mitral stenosis and hyperthyroidism. Montier employs the following formula: Neutral physostigmin salicylate 0.01 gram, glycerin 3.5 c.c. and distilled water 1.5 c.c. to which is added sufficient alcohol to make 10 c.c. He begins with 10 drops and gradually increases to 60 drops and then reduces in the same way. He never exceeded 60 drops of this mixture.

**Ether.** Attention has been called in previous issues to the danger of administering ether to individuals who are definitely tuberculous or those in whom there is reason to suspect this condition.

In spite of the repeated warnings of this danger, many surgeons still persist in using ether as an anesthetic. A year or so ago an article appeared in which the statement was made that the inhalation of ether had a distinctly beneficial effect on *pulmonary tuberculosis*. This is absolutely at variance with the clinical experience of those who see many cases of tuberculosis. Indeed it is remarkable how many patients date the onset of their pulmonary trouble to an operation, often trivial in nature, in which ether was the anesthetic employed. In an experimental study, Rogers<sup>132</sup> found that guinea-pigs infected with the tubercle bacillus failed to show any improvement as the result of ether anesthesia. It does not possess any inhibitory action on the progress of tubercle formation, nor does it prolong the life of the animal.

Intramuscular injections of ether have been added to the long list of remedies used in the treatment of *whooping-cough*. Andrian<sup>133</sup> injects 1 c.c. of ether in infants and 2 c.c. in older children on alternate days. He states that he has always found it successful in arresting

<sup>130</sup> Bull. de la Soc. méd. des hôp., June 11, 1920.

<sup>131</sup> Arch. des mal. de l'Appareil Digestif, April, 1920.

<sup>132</sup> Ohio State Medical Journal, July, 1920.

<sup>133</sup> Bull. de la Soc. méd. des hôp., June 11, 1920.



the disease except when adenoids are a factor in the spasmodic coughing. He ascribes the benefit of the ether to its disinfecting properties.

The use of ether has also been advocated by Lascalle<sup>134</sup> in the treatment of *bronchopneumonia* in children. He advises the injection of 1 c.c. of ether every four hours; in some cases an injection night and morning is sufficient, and often one injection is enough. He says he has employed this method of treatment in over 200 cases and has never noted any ill-effects. According to Lascalle, the injected ether leaves the body through the lungs, and being a powerful disinfectant is capable of impairing the vital conditions of the microbes in the lungs. The result of the treatment depends less on the quantity than on the time at which the treatment is started. The earlier in the disease the ether is given, the better the results.

**Guaiacol.** The use of one of the guaiacol group in the treatment of *pulmonary tuberculosis* has long been recognized. Many have claimed for this drug distinct advantages. DeWitt, Luyenaga and Wells<sup>135</sup> state that while they failed to observe any beneficial therapeutic effect on tuberculous guinea-pigs this was to be expected in view of the low bactericidal power of this group. This does not mean, however, that guaiacol and its congeners may not be of value in open tuberculous infections in man in which bacteria other than the *Bacillus tuberculosis* are involved. They do feel that their experiments confirm the opinion which seems to have been reached by careful clinical observers, that creosote and guaiacol do not exert a specific action on tuberculosis.

**Heliotherapy.** The application of heliotherapy by the Thézac-Porsmeur method has been tried by Lovett<sup>136</sup> in the treatment of *chronic suppurative conditions of the bones and joints*.

The essential feature of the treatment is the concentration of the sun's rays by means of a double convex lens with a diameter of 12 inches and a focal length of 72 inches. At the focal point the heat is very great as it would be in any lens used as a burning glass. As a rule, the patient should be placed at a point where the sun's rays form a circle of from 3 to 5 inches in diameter. As the patient is moved further away from the lens, the heat increases, and as the patient is moved nearer the lens, the heat diminishes.

The lens is mounted in a canvas cylinder 1 foot in diameter and 3 feet in length, which is kept rigid by two circular wires with thin strips of wood running from one hoop to the other, over which the canvas is stretched. The lens is placed a few inches from one end of the cylinder. The advantage of the cylinder is that the lens may be pointed directly at the patient, thus making the application of the treatment more definite. The cylinder is mounted on a tripod and can be swung in any direction by means of a handle.

The first treatment should last for five minutes and increased for five minutes up to thirty minutes daily. The skin around the wound is,

<sup>134</sup> Arch. de méd. des enfants, July, 1920.

<sup>135</sup> Journal of Infectious Diseases, August, 1920.

<sup>136</sup> Journal of the American Medical Association, April 3, 1920.

as a rule, protected by towels, and the individual giving the treatment should wear colored glasses, as the light is extremely bright. The eyes of the patient should also be protected from the glare. In one case the treatments, for a time, were continued for an hour and a half without any ill effects.

Lovett states that the effect of the treatment on suppurating wounds was perfectly definite: (1) The discharge immediately increased and then diminished; (2) pale granulations took on a healthier color; and (3) sensitiveness diminished. The method was thoroughly tested by selecting a series of suppurating wounds of the severest type and obviously difficult.

In Lovett's opinion, this method of treatment showed greater progress than there had been before or than there had been in similar cases. He states that for six years he has been a strong advocate of the value of exposing the whole body to the sun's rays and that he is convinced that the treatment with the lens is not only a distinct addition to our therapeutic measures, as it possesses decided advantages. It can be regulated and controlled; it is applicable when the sun is sufficiently obscured to be useless for general exposure; and it can be used in a sunny room by opening the window and pointing the cylinder at the sun. If used properly, it is free from a risk.

A bacterial count made from the wound discharge showed that the effect of the sun treatment was to lower immediately the count. In several cases when there was an underlying suppuration the count naturally was not affected.

Lovett believes that the value of the method was apparently demonstrated in cases of chronic suppuration from *tuberculosis*, *syphilis* and *chronic osteomyelitis*.

The value of heliotherapy in the treatment of female *genital tuberculosis* is reported on by Exchaquet.<sup>137</sup> He employed this method in 20 cases. In 8 cases the treatment was continued to a complete cure, averaging thirty-three weeks. In the others the patients were satisfied with the results obtained in thirteen weeks on an average, and did not continue. Mixed infection did not do well as three cases with a superimposed colon or gonococcus infection flared up under its use. In cases of salpingitis operative interference should always be kept in mind.

**Hexamethylenamin.** In the treatment of jaundice associated with acute infection, Weil<sup>138</sup> gives systematically daily by the drop method, by the rectum, 1.5 gm. of hexamethylenamin in a solution of sugar, 45 gms. to 1 liter of boiled water. Sometimes he adds a little epinephrin.

Weil believes that this method is more effective than injection into a vein or the subcutaneous tissues. It stimulates the liver and kidneys and induces intense diuresis, while the sugar promotes the production of glycogen and the elimination of nitrogenous waste and brings about a more profuse flow of bile. He employs sugar instead of glucose as the former is more readily obtained. This treatment he states may transform conditions with jaundice from gall-stones, so that operative

<sup>137</sup> Revue Française de Gynécologie et d'Obstétrique, March, 1920.

<sup>138</sup> Bull. méd., Paris, April 21, 1920.

measures may become unnecessary. It fails when the jaundice is due to cirrhosis of the liver or to neoplasms and should not be employed in dysentery.

**Humanol.** The prevention of adhesions following abdominal operations or operations or accidents involving the tendons is a matter of great concern to the surgeon. Many methods have been employed in trying to avoid peritoneal adhesions, but, so far, none of those tried has proved very satisfactory. Laeffler<sup>139</sup> has made a preliminary report on the use of fluid human fat (humanol). The humanol is obtained from fatty tissues secured at operations (abdominal fat, lipomas, etc.). After all the connective tissue is removed, the fat is then heated for three hours over a water-bath and filtered. Only the fat obtained from healthy individuals is used.

After a tendon or nerve has been freed from adhesions and hemorrhage stopped, the wound is closed, leaving a pinhead opening just large enough to admit the top of a syringe. The suture is then drawn lightly, the humanol is injected and the suture is then tied. The wound heals readily and the resulting scar is soft and elastic. The humanol is particularly serviceable in injuries involving the hand and fingers. It is also of service in joint injuries and in certain forms of chronic arthritis.

Laeffler has also used an "iodoform humanol" (5 or 10 per cent.) in the treatment of tuberculosis of the bones and joints.

**Hydrochloric Acid.** Bastedo<sup>140</sup> states that in cases of *achylia gastrica*, whether or not accompanying pernicious anemia, a deficiency of acid may be partially overcome by hydrochloric acid medication. In the achylia with diarrhea, the acid generally gives better results than in the achylia without diarrhea. When the acid produces sourness and stomach irritation, its use should be discontinued. To avoid acidosis, alkalies should be given during the same period, though not at the same time as the acid. The amount of alkali used should be judged by the effect on the urinary reaction.

For digestive purposes, hydrochloric acid should always be accompanied by pepsin.

Stratford<sup>141</sup> reports the case of a man who swallowed about 3 ounces of dilute hydrochloric acid following the taking of a heavy meal. This was discovered a few minutes later and he was promptly given a tumblerful of hot water and mustard. He vomited, and continued to do so, bringing up much dark brown material with mucus and blood-stained froth.

He was given milk and sodium bicarbonate and later a paste of bismuth carbonate in albumen-water both by mouth and by rectum in view of a possible acidemia. In addition, stimulants (strychnine and caffeine) and morphine were given. He slowly recovered without serious complications.

**Iodine.** One of the most annoying infections which hospitals for children have to deal with is *vulvovaginitis*. Once this infection gains

<sup>139</sup> München. med. Wochenschr., November 7, 1919.

<sup>140</sup> American Journal of the Medical Sciences, January, 1920.

<sup>141</sup> British Medical Journal, July 31, 1920.



entrance into a children's ward, it spreads with the greatest rapidity in spite of all precautions. In addition, it is often an obstinate infection to deal with in the child herself. As Bland<sup>142</sup> states, many cases respond fairly promptly to treatment and tend to a favorable result; in others, despite every measure, the trouble persists and recurs. His method of treatment is to cleanse the vulva and vagina with large quantities of warm water for a period of two or three days. This is accomplished through a No. 14 soft rubber catheter. After gaining the confidence of the child, he employs Lugol's solution of iodine in warm water. He begins with a weak solution, usually one-quarter of a teaspoonful to two quarts of warm water, or approximately one-quarter of 1 per cent. This is gradually increased to 1 per cent. The vulva is first thoroughly cleansed with this preparation, after which the catheter is introduced into the vagina and this canal is thoroughly flushed—no special amount is used. The solution is allowed to run until it returns absolutely clear, but not less than one gallon is used at a sitting. The irrigation is carried out morning and evening and continued for at least the first three or four weeks. In addition, once daily a 25 per cent. solution of *argyrol* is instilled into the vaginal canal. Usually 20 minims or a medicine dropper completely filled is quite sufficient. At the same time, the vulva is also painted with this material, and a cotton pad moistened with 25 per cent. *argyrol* is placed in contact with the labia and vestibule. At the expiration of a month or six weeks, the irrigation is used only once a day, but the application is carried out daily. This treatment is continued until four successive negative smears are returned and also until the complement-fixation test is negative.

The use of iodine in the form of vapor has been investigated experimentally by Luckhardt, Koch, Schraeder and Weiland.<sup>143</sup> Introduced intratracheally in the form of fumes, the iodine is rapidly and completely absorbed; but it was found that the administration of the fumes by inhalation, even in small quantities, is dangerous. In small quantities it produces dyspnea; and when given in large quantities, acute and fatal edema occurs within twenty-four hours. If respiratory disorders are present, the edema develops very quickly. So far, they have not been able to control the dosage.

They also found that the effects of iodine fumes produce, in dogs, the same necropsy changes as those following the inhalation of bromine or chlorine gas in men.

**Kaolin.** The use of kaolin or *bismuth subnitrate* for gastric pain instead of sodium bicarbonate is recommended by Hayem.<sup>144</sup> In using the bismuth, he gives one single large dose (20 gm.) in the morning, fasting. He has never noted any toxic effects from the bismuth. Kolin is equally effective.

<sup>142</sup> New York Medical Journal, March 20, 1920.

<sup>143</sup> Journal of Pharmacology and Experimental Therapeutics, March, 1920.

<sup>144</sup> Bull. de l'Acad. de méd., March 9, 1920.

**Lemongrass Oil.** This oil is recommended by Takasugi<sup>145</sup> in the treatment of skin diseases due to animal parasites. The principal toxic ingredient against insects in lemongrass oil appears to be citronella.

**Luminal.** This drug belongs to the group containing adalin, barbital and barbital sodium. Dercum<sup>146</sup> recommends it highly in the treatment of *epilepsy*. At first he employed the drug in divided doses three times daily, as is done with the bromides. He found, however, that this method of administration sometimes made the patient a little heavy during the day and at times even a little dizzy. After employing the drug for a time, he found that if he gave one dose at bedtime these untoward symptoms did not occur, while the efficiency of the drug was in no way impaired, if indeed it was not enhanced. Even in confirmed epileptics, the drug exercised a remarkable control over the seizures which were usually inhibited altogether. The doses required for this purpose were exceedingly small;  $1\frac{1}{2}$  to 2 grains usually sufficed, and it was rare that as much as 3 grains were required.

Dercum found that in some cases luminal did not at once control the seizures, and might have to be given for a week or two before its full action was established. In addition, Dercum found that the use of small doses of the bromides three times daily for ten days or two weeks established the action of the luminal more promptly.

His method of treating epilepsy is as follows: Instructions regarding diet, namely, the diminution of the amount of red meats and carbohydrates and the avoidance of stimulants of all kinds (tea, coffee, etc.); seeing that the avenues of elimination are kept open (bowels, kidneys and skin). Moderate doses of a laxative water are given in the morning, the patient is instructed to drink freely of water during the day and a tepid sponge bath taken once daily. Bathing in a tub is forbidden for obvious reasons.

In regard to medication, he prescribes, on the average, 20 grains of sodium bromide three times daily after meals, and  $1\frac{1}{2}$  grains of luminal at bedtime. As a rule, the epileptic seizures disappear promptly, and in the course of a few days the bromides can be reduced by a half and finally discontinued. The luminal is continued indefinitely. In many cases it is given for months, and in a few instances over a period of one, two or even more years. Dercum states that he has never seen the slightest deleterious influence upon the mental life of the patient.

If a bromide is employed, Dercum prefers *sodium bromide* and during the time of its administration he withdraws sodium chloride from the diet; he believes that during the sodium chloride withdrawal, the sodium bromide replaces the former in the tissues. Luminal is most effective in the group of "essential" or "morphologic" epilepsies, but it is also of great value in other forms of epilepsy.

The value of luminal in the treatment of epilepsy is also endorsed by Grinker.<sup>147</sup> He found that small doses from  $1\frac{1}{2}$  to 2 grains once or

<sup>145</sup> Bulletin of Naval Medical Association of Japan, February, 1920.

<sup>146</sup> Therapeutic Gazette, September, 1919.

<sup>147</sup> Journal of the American Medical Association, August 28, 1920.



twice daily, were capable of causing an arrest of the convulsions in epilepsy and that while large doses may be given safely, they are seldom required. Large doses may be given when beginning treatment, especially after the sudden withdrawal of the bromides, but the dose may then be gradually reduced to  $1\frac{1}{2}$  or 2 grains. The drug is apparently harmless, even after prolonged administration, and does not lead to habit formation. In addition, the mentality of patients taking luminal does not show the peculiar torpor of those taking bromides.

**Mercury.** As the result of considerable agitation and the introduction of additional safeguards, the ingestion of bichloride tablets, whether accidentally or with suicidal intent, is becoming less and less frequent. An additional source of danger still remains, however. On several occasions reference has been made to the use of bichloride of mercury tablets by women as a vaginal injection. The absorption of the drug and the subsequent symptoms are identical with those which follow the ingestion of the drug.

Bland<sup>148</sup> reports 3 cases in which vaginal douching with a strong solution of mercuric chlorid led to severe symptoms of poisoning. Two of these cases ended fatally. In addition to the general symptoms of mercurial poisoning, a very severe local reaction occurs. In the non-fatal case the vulva was swollen and inflamed four weeks after the injection. The vagina showed most striking changes. The canal was almost completely closed, and its diameter would not admit the introduction of the index finger. The mucosa had entirely sloughed away and the canal was lined by red, resistant, tender and granular membrane. There were no marked constitutional symptoms at this time.

A case similar to those of Bland's is reported by McPeck.<sup>149</sup> Extensive sloughing occurred and portions of the vaginal mucosa were detached in large pieces. The woman recovered, but four months later the urine showed the presence of albumin and casts.

Albaugh<sup>150</sup> calls attention to the relative frequency of mercurial poisoning in certain trades, particularly in the preparation of mercurial salts and the felt-hat industry. The poisoning is usually chronic, and is caused by the inhalation of small quantities of vapor.

The symptoms of *industrial mercurial poisoning* are not unlike the symptoms of mercurialism from therapeutically administered mercury. There is usually a marked increase in the flow of saliva, with foul breath and a metallic taste in the mouth. There may be a simple inflammatory condition of the gums, or it may go on to ulceration with loosening of the teeth. The more important symptoms, however, are the psychoses and nervous afflictions, which are usually accompanied by digestive derangements and loss of strength. Patients frequently exhibit a marked tremor before other symptoms manifest themselves. It is not unusual after long-continued exposure or repeated attacks of poisoning for the patient to become emaciated, with anemia, loss of strength, muscular atrophy and disturbed digestion. Such cases may

<sup>148</sup> Journal of the American Medical Association, May 1, 1920.

<sup>149</sup> Ibid., September 4, 1920.

<sup>150</sup> Modern Medicine, November, 1919.



result fatally. Slight cases of mercurialism usually recover, however, if the patient is removed from the influence of the poison.

Prevention of mercurial poisoning depends upon the confinement or removal of mercurial vapor and mercury dust as well as strict personal hygiene, particularly proper care of the mouth. In the hatters' and furriers' trades the danger arises chiefly in cutting, dressing, drying, sorting, and in the subsequent stages of felt-hat manufacture. The prohibition of entry into drying rooms while drying is going on and the removal of vapors and dust at the points of origin are important. The treatment of mercurial poisoning is symptomatic. Patients should be removed from exposure with the first symptoms. Potassium chlorate mouth-wash may be used for the inflammatory condition of the mucous membrane. Effort should be made to promote the general condition by strengthening food. Baths and electricity should be resorted to for the nervous symptoms.

The treatment of *syphilis* by means of the intravenous injection of mercury in the form of *mercuric iodid* is recommended by Spittel.<sup>151</sup> He has given over 4000 of these injections and believes the method a valuable adjunct to the treatment of syphilis with arsphenamin.

The solution he employs is as follows: Mercuric chlorid, 50 grains; sodium or potassium iodid, 8 drams; phenolphthalein (0.5 per cent. solution), 20 minims; sodium hydrate (25 per cent. solution), about 2 drams; distilled water to 40 ounces. The dose for an adult is from 8 to 12 c.c. intravenously. In nervous syphilis, this method is particularly valuable.

An ordinary case of secondary syphilis may be treated with five or six injections each of arsphenamin and mercuric iodid given, alternately, at intervals of from seven to ten days. If a permanent negative Wassermann is not obtained, additional courses should be given.

The treatment of *syphilis associated with tuberculosis* has been the subject of considerable comment during the past few years. It has always been held by many that tuberculous patients do not tolerate mercury well, and this, I think, is still the prevailing opinion. Elliott,<sup>152</sup> in reporting a series of cases showing this combination, concludes that mercury should be used with care and that while no immediate bad effects are noted, untoward symptoms may appear months later. In his opinion, *arsphenamin* is the drug of choice in these cases. He believes, however, that the dose should be smaller and the interval longer, as otherwise a full dose may stimulate the tuberculous foci. At the Phipps Institute we follow this plan for a time. If no increase in the tuberculous symptoms occurs, we then proceed as in the ordinary uncomplicated case. Of course, greater care is needed in those actively tuberculous than in those with a latent or arrested lesion.

The use of *potassium mercuric iodid* as a skin disinfectant is recommended by McKenna and Fisher.<sup>153</sup> As a result of experimental work, they found that potassium mercuric iodid, in a concentration of 1 to 100

<sup>151</sup> Lancet, February 14, 1920.

<sup>152</sup> American Journal of Syphilis, April, 1919.

<sup>153</sup> Surgery, Gynecology and Obstetrics, April, 1920.

in acetone, or in 70 per cent. alcoholic solution, is more efficient than the official tincture of iodine. It is free from any harmful action and is equally efficacious in killing bacteria on and in the skin. An additional advantage is that this solution does not stain, nor does it cause irritation or blistering of the skin.

Reference has been made in PROGRESSIVE MEDICINE in previous years to the use of *calomel* in the treatment of *pruritus ani* and external hemorrhoids. A note on this method has been published in the *Indian Medical Gazette* (June, 1919). The calomel is dusted on the anus and its neighborhood after defecation, forming a white lacquer, traces of which are still visible twenty-four hours later. It is not necessary to incorporate the calomel in an ointment, as a matter of fact this method is much less effective than when used as a dusting powder. In addition to relieving the itching of the *pruritus ani*, the pain of the hemorrhoids quickly ceases and after a few applications the hemorrhoids shrink and are converted into pale, indolent flaps of skin.

The treatment of *ileocolitis* with calomel is advised by Womack.<sup>154</sup> He gives from  $\frac{1}{24}$  to  $\frac{1}{48}$  of a grain of calomel and from  $\frac{1}{50}$  to  $\frac{1}{125}$  of a grain of morphine by mouth every three hours, until the spasm of the bowel quiets down. In his opinion, the *ileocolitis* is mainly due to a gas-producing organism that is an attenuated or malignant form of the colon bacillus. There is also an accompanying pyelitis due to the colon bacillus. He believes therefore that attention should be paid to the kidneys by feeding a selected carbohydrate diet and the administration of plenty of water.

Recently, *calomel ointment* has been advocated as a substitute for the old fashioned *blue ointment*. Calomel ointment has been used for inunction purposes because of its cleanliness, and also because it was claimed that it was equally efficient and free from the danger of causing mercurial poisoning. Cole and Litman,<sup>155</sup> in reporting 54 cases in which calomel ointment was used, condemn this preparation as a substitute for blue ointment. They state that the rarity of salivation and soreness of the gums is not an indication of safety, but shows that it does not enter the body as readily. This is an important point as mercurial inunctions are usually employed for the purpose of obtaining a quick and a maximum effect of the drug. If calomel ointment fails in this particular, it loses its claim as being superior to the blue ointment. Certainly the danger of salivation is less than the unchecked progress of the syphilitic lesions.

Gordin<sup>156</sup> calls attention to the promiscuous use of calomel in the South. He believes that it is no exaggeration to state that calomel is used in 90 per cent. of all diseases. The laity use it freely on their own account; druggists freely recommend it; and physicians themselves are entirely too lax in their use of the drug. Gordin reports 2 cases of severe *mercurial stomatitis* caused by the administration of calomel. In both instances, the dose was not excessive but was followed by a

<sup>154</sup> Southern Medical Journal, July, 1920.

<sup>155</sup> Therapeutic Gazette, 1920, p. 247.

<sup>156</sup> Journal of the American Medical Association, April 24, 1920.



stomatitis in which gangrenous patches occurred. In 1 case nearly the entire right cheek sloughed away and all but one or two teeth loosened and fell out.

Under certain conditions, and particularly if the kidney function is impaired, small doses of calomel will often give rise to severe stomatitis and salivation. I recall a case at the Philadelphia General Hospital in which the use of a popular diuretic pill containing a grain each of digitalis, squill and calomel gave rise to a violent stomatitis.

In a study of the effect of calomel on the kidneys and the duration of its excretion, Beinhauer<sup>157</sup> found that the excretion of calomel in ordinary therapeutic doses begins within six to twelve hours and is continued until the sixth day, depending upon the size of the dose. A small dose of the drug is excreted as rapidly as a larger dose, but over a shorter period of time. In so far as he could determine by the urine analysis, calomel is excreted without injurious effects upon the kidneys.

**Nitrohydrochloric Acid.** Hare,<sup>158</sup> in an editorial article, takes exception to the statement made by a writer that nitrohydrochloric acid "hardly seems worthy of a place in the *Materia Medica*." He points out that he was taught by the late H. C. Wood that in certain conditions of hepatic torpor strong nitrohydrochloric acid in the dose of 5 drops, diluted with water at the time it is taken, is exceedingly useful. According to Wood, English physicians in India found the drug of value as a hepatic stimulant when given internally, but also, when diluted with water, in compresses over the liver in the treatment of the hepatitis of hot climates. Wood also pointed out that in many cases of impaired digestion with great mental depression, almost bordering on a true melancholia, the use of nitrohydrochloric acid often produced remarkably good results, particularly if the examination of the urine showed an excess of oxalate crystals. Hare states that the acid will often clear up a foul tongue, a torpid liver and remove mental depression when calomel fails, and, what is more, if given freely, in some cases the patient after a few doses will develop a relaxed state of the bowels or a diarrhea associated with an increased secretion of bile. He states that he has long taught that while hydrochloric acid is neither astringent nor particularly stimulating, and that while nitric acid is astringent, nitrohydrochloric acid, of all chemical acids that are used in medicine, is laxative and non-astringent in its effects.

**Novarsenobenzol.**<sup>159</sup> Attention has been directed to the use of this drug in the treatment of *influenza*. It was first used by Bruhl and Frank<sup>160</sup> on the hypothesis that arsenic being a powerful parasiticide when employed against spirochetes it might be of use in influenza as for a time it was thought possible this disease might be of spirochetal origin. They first used the drug by mouth in the form of compressed tablets, each containing 10 centigrams of novarsenobenzol, in the daily dose of three to four tablets, in cases in which the influenzal symptoms

<sup>157</sup> American Journal of the Medical Sciences, June, 1920.

<sup>158</sup> Therapeutic Gazette, August, 1920.

<sup>159</sup> New York Medical Journal, November 8, 1919.

<sup>160</sup> Quoted in Therapeutic Gazette, 1920, p. 183.



continued for a fortnight or more. Some patients took in all 5 grams, or even more, without any untoward effects.

In the more severe forms of influenza, the drug was given intravenously in the dose of 30 centigrams; this was repeated according to indication two or three days in succession or with an interval of two or three days. When an interval of several days intervened between injections, the drug was given by mouth. Of 38 cases of influenza treated by Bruhl and Frank, there were 8 deaths. It is their belief that the death-rate in this series would have been higher had the novarsenobenzol not been used.

Hare<sup>161</sup> employed *arsphenamine* in the treatment of influenza.

Fortunately, influenza comes only at wide intervals of time, and, unfortunately, each epidemic finds the physicians utterly unprepared to cope with it. This has certainly been true of the last three great pandemics. Those who went through the pandemic of 1889-90 had had no experience with the previous one in 1848. Physicians in 1889-90 were dealing with, to them, a new disease. The same thing was true of the last pandemic. Most of the present-day physicians had had no experience with the previous outbreak, and those who had seemed to be as greatly at sea as to what to do as those with no experience. The truth of the matter seems to be that these great pandemics, especially at their height, are practically uncontrollable and must burn themselves out. It is difficult to measure the effects of therapeutic agents as, in some instances, they are employed at a time when the virulence of the epidemic is subsiding. The treatment that is successful at this stage of the disease might have but little value if given earlier. Beaumont,<sup>162</sup> in commenting on the various therapeutic measures employed in the treatment of influenza, states that in the present state of our knowledge symptomatic treatment alone is available.

**Picric Acid.** The use of iodine as a skin disinfectant prior to operative interference is now an almost universal procedure. Cassegrain<sup>163</sup> first saw picric acid employed as a preoperative disinfectant in the British Army. In his work, he modified the original technic, as follows: (1) By wiping the skin with alcohol and (2) painting it with 5 per cent. picric acid. He omitted the washing with soap and water as a time saver.

In Cassegrain's experience, the picric acid can be used with soap and water; it does not irritate the skin and it is approximately 40 per cent. cheaper than the drug now almost universally used for the same purpose.

**Pituitrin.** The use of this substance is now thoroughly established in obstetrical practice, but it is well to keep in mind that it is not entirely free from danger. The indiscriminate use to which pituitrin was put several years ago has largely ceased, although it is probable that the need for caution in its employment is still in need of being emphasized. Alice F. Maxwell,<sup>164</sup> in reporting a fatal case of rupture of the uterus,

<sup>161</sup> United States Naval Marine Bulletin, October, 1919.

<sup>162</sup> Practitioner, April, 1920.

<sup>163</sup> New Orleans Medical and Surgical Journal, January, 1920.

<sup>164</sup> Journal of the American Medical Association, May 15, 1920.

states that in her case the pituitary extract was employed in a conservative manner; was administered in the presence of well-established indications and in doses well within the limits of safety. She is convinced that there is danger in the indiscriminate use of pituitrin, especially in the dose ordinarily recommended, namely, 1 c.c. ampules. Even when employed for the strictest indications and in small doses, complications may arise so rapidly that they cannot be met adequately even in well-equipped hospitals. One thing is certain, which is that pituitrin has no place in the conduct of normal labor. The drug should be limited to cases of uterine inertia coming on when the head is well engaged without disproportion between the child and the mother's pelvis, with complete dilation of the cervix and without undue thinning of the lower uterine segment. The dose should be a third of an ampule and repeated if needed. The figures indicating the frequency of rupture of the uterus following the use of pituitrin vary greatly—from 1 in 250 cases to 1 in every 2114 cases. As Maxwell points out, the figures do not show the true frequency as they are all compiled from hospital statistics. It must be true that the woman often succumbs at once at home or else suffers the immediate shock of an incomplete rupture to die later, when the delayed death is incorrectly ascribed to peritonitis or some other condition.

Schulze<sup>165</sup> also emphasizes the fact that pituitrin is not free from danger. It should never be used in the first stages of labor. It has no place in any stage in a normal case. It should not be used to induce labor at full term, but it may be employed to hasten the termination of an inevitable abortion. Schulze states in a healthy multiparous woman with os fully dilated and the membranes ruptured, with a head presenting normally, resting on a relaxed and easily stretched perineum, and the pains showing a tendency to lag, one has conditions as nearly ideal for the administration of pituitrin as we can hope to find them. He states that the age and parity of the woman must be kept in mind. Advancing years and repeated pregnancies and labors, especially at short intervals, produce degenerative changes in the muscle fibers of the uterus. As a consequence, a uterus of this type does not stand the strain of labor well. Either they do not exert themselves sufficiently to terminate labor spontaneously, or they may rupture. In either case the muscle is not up to par, and the use of pituitrin would be an unusually hazardous procedure.

Stein<sup>166</sup> is in favor of the use of small doses of pituitrin (2 or 3 minims), given intramuscularly, and inhalations of nitrous oxide to facilitate the labor and mitigate the discomfort.

In addition to its use in obstetrics, pituitrin has been of the greatest service in the treatment of *diabetes insipidus*. The reports made so far show that it rarely fails in giving symptomatic relief. Flandin,<sup>167</sup> and his associates, report the case of a very obese woman suffering from diabetes insipidus. Although no effect was produced on the obesity, the

<sup>165</sup> The Journal-Lancet, November 1, 1919.

<sup>166</sup> American Journal of Obstetrics, October, 1919.

<sup>167</sup> Bull. de la Soc. méd. de hôp., April 16, 1920.

pituitrin promptly proved effectual so far as the polydipsia and the polyuria were concerned.

A case of diabetes insipidus treated with *pituitrin* hypodermically is reported by Schnabel and Gerhard.<sup>168</sup> Two years have elapsed since the cessation of symptoms.

Schulze<sup>169</sup> points out that, in addition to the above indications, pituitrin can be used to advantage for intestinal distention and retention of urine. When combined with ergotal, it can be used for the control of postpartum hemorrhage and in cases of Cesarean section.

**Protein.** In certain types of *arthritis*, Gow<sup>170</sup> states that he has obtained good results from intravenous protein therapy. He states that the vaccine is given entirely for a shock effect. The type of arthritis which responds best to this method is the multiple infective form for which no active source of primary infection or septic absorption is demonstrable. He has also found that *peptone* intravenously in conjunction with sensitized vaccine subcutaneously is of value in cases of streptococcal septicemia.

Gow makes no extravagant claims for the use of protein in these conditions, but asserts that it may be used as an accessory weapon in association with other remedies.

**Quinine.** This drug, in common with digitalis, is always the subject of frequent communications. Although to be regarded as a specific in the treatment of *malaria*, with the possible exception of the very malignant forms, quinine is the subject of endless discussions as to dosage, the particular salt to be employed and the method of administration.

An editorial article<sup>171</sup> gives a brief account of the history of *cinchona*. The drug was introduced into Europe in 1640. In that year the Count of Chinchon, who was at that time viceroy of Peru, returned to Spain with his wife, who took with her a quantity of the medicinal cinchona bark. The year 1920 marks the centenary of the first isolation of the most valuable alkaloid of cinchona bark (quinine) by Joseph Pelletier. To show the enormous increase in the production of the quinine salts, it is recalled that in 1826 Pelletier and Levaillant together, made about 390 pounds of the salts of quinine. During the year ending in June, 1914, the United States alone imported cinchona bark to the amount of 3,648,868 ounces, valued at \$464,412 and quinine sulphate and other alkaloids or salts of cinchona bark to the amount of 2,879,466 ounces, valued at \$624,125. What the introduction of this medicine has meant in localities where malaria is constantly prevalent need not be enlarged upon; it is hardly to be measured in dollars.

Mayne and Carter<sup>172</sup> assert that the greatest faults in dealing with malaria are insufficient dosage and too brief a time. In many localities it is the custom to administer to an adult, with active malaria 12 to

<sup>168</sup> New York Medical Journal, May 8, 1920.

<sup>169</sup> Loc. cit.

<sup>170</sup> British Medical Journal, February 28, 1920.

<sup>171</sup> Journal of the American Medical Association, March 13, 1920.

<sup>172</sup> Ibid., October 11, 1919.



20 grains daily, and when the clinical symptoms disappear the treatment is discontinued.

Treatment, to be effective, must provide: (1) For the relief of the patient, namely, the elimination of clinical symptoms; (2) for the destruction of the plasmodia in the peripheral circulation tending toward the prevention of the formation of sexual parasites; (3) for the prevention of the production of quinine-inaccessible parasites (so-called resistant or quinine-fast forms); and (4) for the effectual inhibition of the recurrence of clinical symptoms accompanying a relapse with the re-invasion of asexual parasites.

To gain these ends, Mayne and Carter propose the following plan which provides for the administration of quinine for a minimum of seventy-five days. The total amount given is 800 grains of quinine bisulphate in four courses of 200 grains each.

1. *Forty Grains Daily for Five Days.* Ten grains of quinine bisulphate should be given four times daily. At the end of this period there should be no severe paroxysms, no chills, and only young rings and mature gametocytes in the blood.

2. *Twenty Grains Daily for Ten Days.* About the middle of this stage the patient should probably be out of bed and clinically and apparently normal; fevers and chills probably absent. With the exception of gametocytes, parasites will not be demonstrable microscopically.

3. *Ten Grains for Twenty Days.* Arsenic (Fowler's) or other tonic may be prescribed, if indicated. Only gametocytes remain in the microscopic examination. The patient should be on duty or able to resume normal activities, if necessary.

4. *Five Grains for Forty Days.* In this stage, not the least important, a 5-grain capsule of quinine bisulphate or its equivalent should be taken with a tonic accompaniment if indicated. This stage is marked by the apparent recovery of the patient. At this juncture a continuance of treatment should be strongly urged, especially in the benign types of malaria, for a period of two weeks or more. By this time a microscopic examination reveals only rapidly disappearing or disintegrating gametocytes which may be considered potentially negligible. The sexual forms of tertian and quartan parasites are not demonstrable at this stage.

In young persons and in chronic cases among adults, the amount of the quinine should be reduced. They realize that the weak point in the treatment is in inducing the physician and patient to continue the treatment sufficiently long to insure against the danger of a relapse.

Cowan and Strong<sup>173</sup> emphasizes the importance of keeping patients in bed during the continuance of the fever and for some days afterward. They state that a too early resumption of activity is a common cause of failure to overcome the infection. The diet should be fluid and easily digestible and the bowels freely moved.

The quinine should be given as soon as the diagnosis is made, whether

fever is present or not. They prefer the *bihydrochloride*, *hydrochloride* or the *hydrobromide* salts. They may be given in solution, in powder form, in capsule, or in cachets. Pills and tablets are to be avoided as they are often too hard and relatively insoluble. If the sulphate of quinine is used, an acid should be added to insure solution and an aromatic to make the solution more palatable.

Cowan and Strong administer 45 grains daily on the average. According to the severity of the case, the initial dose may be 30 to 60 grains daily. This is continued while the fever lasts and for from three to seven days longer. The dose may then be reduced to 30 grains and continued until the patient has been afebrile for at least twenty-one days. They divide the daily amount into three doses given after meals. If fever is present, it is often helpful to give the drug at four-hour intervals. Intolerance to the drug is rare, except in the presence of gastro-intestinal symptoms. Tinnitus and deafness can generally be ignored. The latter symptoms are less troublesome if the hydrobromide is used, or if bromide of sodium is added to the mixture.

Oral administration of quinine is contra-indicated in cases in which gastro-intestinal symptoms (vomiting, diarrhea, dysentery) are present, and in cases in which the tongue is thickly coated. When this is the case the drug is given intramuscularly or intravenously, mention of which will be made presently. The value of quinine in controlling acute malaria and of relieving cerebral symptoms is in marked contrast with its failure, in many instances, to prevent relapses of the disease. In regard to prophylaxis against relapses, Phear<sup>174</sup> calls attention to the plan followed by Anderson, in Macedonia. Of all the methods tried, that of the so-called week-end system gave the best results. This plan calls for the administration of 30 grains of quinine on each of two successive days each week. This increased the percentage of non-relapse cases to 78, as compared with 32 per cent. in the control series, in which no quinine was given after the initial pyrexia had subsided. In patients who are at work, the same weekly quantity of quinine distributed in daily doses of 10 grains daily for six days a week has undoubted advantages over the week-end method.

The advisability of administering *quinine intramuscularly* or *intravenously* continues to be discussed. It will be recalled that Bass's views on the oral administration of quinine were reviewed in *PROGRESSIVE MEDICINE* for last year. He feels that any other method, than the oral, is rarely needed, and if those who advise the intramuscular injections were subjected to this method themselves, fewer would be in favor of it. Castellani, whose experience in tropical diseases is great, believes that quinine should be given by mouth in the ordinary cases, intramuscularly in the severe cases and both intramuscularly and intravenously in the pernicious cases.

Cowan and Strong<sup>175</sup> state that if quinine cannot be given by mouth, or the infection is usually severe, intramuscular injections may be given. These are preferable, in their opinion, in cases of massive

<sup>174</sup> Lancet, January 24, 1920.

<sup>175</sup> Loc. cit.

infection, as shown on the blood-film, in patients with cerebral symptoms, however slight, or pulmonary or abdominal symptoms and in cases in which the fever is not influenced by oral administration. For some reason not clearly understood, fever not infrequently persists so long as the drug is given by mouth, but passes off at once when the quinine is given intramuscularly. In some cases it persists in spite of quinine. Cowan and Strong recommend the bihydrochloride for intramuscular injection. It should be dissolved in normal saline solution (10 grains in 10 c.c.) and injected deeply in the gluteal muscles, well away from the sciatic nerve. The needle should be thoroughly emptied before withdrawal and the most scrupulous asepsis must be maintained. Wilcox<sup>176</sup> also advises intramuscular injections in malignant malaria, or in relapsing malaria. For these conditions, a course of from three to six injections should be given, and at the same time quinine should be administered by mouth.

The effect of injections of quinine into the tissues has been studied by Dudgeon.<sup>177</sup> The injection of quinine subcutaneously or intramuscularly, despite the care exercised in giving the injections, give rise to much discomfort and pain. Even with the greatest care a considerable amount of induration, if not actual abscess formation, is likely to occur at the site of the injection. Inasmuch as quinine is a strong protoplasmic poison capable of destroying various forms of animal and vegetable cells, the production of tissue necrosis is not surprising. To avoid this, it has been suggested that dilute solutions be employed. But, according to Dudgeon, a solution so dilute as to avoid edema and tissue necrosis is valueless. He insists on the necessity of realizing that tissue necrosis (edema and local blood destruction) are produced by the solvents frequently employed for quinine administration and the effects are only slightly inferior to those produced by the quinine salts. Extensive damage may take place at the site of these injections and injury to an important nerve trunk may result in a paralysis. Dudgeon warns that repeated intramuscular injections, if the use of this method is deemed imperative, should not be given into the same area of muscle or tissue directly adjacent because otherwise permanent injury of the muscle or associated nerves may result. Wilcox<sup>178</sup> states that his experience with subcutaneous injections of quinine show that sloughing is too apt to occur to warrant this method being employed.

Of late years the intravenous use of quinine has been considerably used. It was first suggested by Baccelli in the severe forms of malaria when life was threatened. There are some who believe that the intravenous method is the one of choice, and should not be reserved for the extremely fatal cases alone. Newton Pitt<sup>179</sup> feels that the method is a simple and valuable one. He does not think that a large amount of fluid must be injected. He quotes the results of Thomson, and

<sup>176</sup> Editorial, *Therapeutic Gazette*, 1920, p. 473.

<sup>177</sup> *Journal of Hygiene*, October, 1919.

<sup>178</sup> *Loc. cit.*

<sup>179</sup> *Therapeutic Gazette*, 1920, p. 471.



others, who have shown that 12 to 15 grains of quinine in 5 to 10 c.c. of fluid have been given intravenously in thousands of cases without ill results.

Patrick<sup>180</sup> states that the assertion that dilute solutions are to be prepared for intravenous injections as the stronger ones may cause venous thrombosis, is not borne out by his experience. He employs a 5 per cent. solution of bihydrochloride made up in distilled water with 0.8 per cent. sodium chloride added. He uses a 20 c.c. Record syringe with a fine needle.

In cases of malaria presenting acute cerebral symptoms, Wilcox<sup>181</sup> asserts that the administration of quinine intravenously is of as much urgency as is the application of surgical measures in cases of fulminating appendicitis, since the delay of a few hours may mean death.

The size of his intravenous dose is 10 grains of the bihydrochloride dissolved in 10 c.c. of normal salt solution, but, if collapse is present, a pint of normal saline is used. For intramuscular injections he gives 10 to 15 grains in 2.5 c.c. of normal salt solution injected deeply into the gluteal muscle.

The advantages of intravenous injections are that they are more efficient in killing the parasite, the drug is more sure to act, and given in this way it may destroy parasites which have become immune to the slowly absorbed doses administered by mouth.

An experimental study of the effects of the usual quinine salts employed for intravenous medication has been made by McCarrison and Cornwall.<sup>182</sup> In large doses the method is dangerous. The respiratory center is more gravely affected than the cardiac. All of the salts of quinine used caused a profound fall of blood-pressure not accompanied by a cessation, or even much diminution, in the strength of the heart-beat, except in two instances in which the respiratory center failed. They advise that the injections should be given very slowly and that great caution should be exercised if the condition of the patient is bad and the blood-pressure is low.

Patrick,<sup>183</sup> who is favorable to the intravenous method, admits that a strong quinine solution may within twenty seconds produce a feeling of uneasiness in the chest and deepening of the respirations, followed by a sensation as if something were rushing inside the head, or a sense of warmth spreading over the body. A bitter taste may appear in the mouth, but all those symptoms, he claims, disappear within a few minutes. He also admits that he has seen hemoglobinuria develop in chronic malaria patients from these injections.

McCarrison and Cornwall state that intravenous injections of quinine should be controlled by blood-pressure observations and that the addition of adrenalin to the solution will counteract, to some extent, the immediate and dangerous fall of pressure. They feel that this method should be reserved for the dangerous forms of malaria and,

<sup>180</sup> Journal of the Royal Army Medical Corps, 1920.

<sup>181</sup> Loc. cit.

<sup>182</sup> Indian Journal of Medical Research, January, 1920,

<sup>183</sup> Loc. cit.

where possible, the hydrobromide, in doses not exceeding 15 grains, should be used; furthermore, there should be added to the solution not more than 0.3 c.c. of the commercial solution of adrenalin in all cases in which the blood-pressure is less than 100.

We feel that their experiments show that quinine is a much more poisonous drug than is generally supposed and that the massive doses so generally employed today cannot fail to depress, by whatever route administered, the cardiovascular and respiratory centers.

Arthweight and Lepper<sup>184</sup> conclude that *blackwater fever* is due to malaria, and that long-standing malarial infections with repeated relapses predispose to it. An attack of blackwater fever is precipitated by a relapse or recurrence of malaria. In their opinion, quinine in the class of cases which they have met has no share in producing blackwater fever, nor has quinine during or after the attack any effect in prolonging or reproducing hemoglobinuria.

In regard to the use of quinine in the treatment of blackwater fever, Phear<sup>185</sup> states that the usual practice has been to withhold it in the absence of definite evidence of active malaria. The presence of parasites in the blood, or of tenderness over an enlarged spleen, has been taken as an indication for quinine, which has been given in effective doses until the malarial manifestations have been brought under control. Later, the use of arsenic is advantageous in promoting blood formation.

In a study of the *metabolism and excretion of quinine*, Nierenstein<sup>186</sup> found that only about half the quinine administered to the human subject is excreted as such in the urine. The remainder, it seems, is metabolized, and two disintegration products, quinitine and hemoquinic acid, were found in the urine. This latter was almost constantly present in the urine of blackwater fever cases, and in much larger quantities than in the urine of ordinary malarial patients.

Quinine sulphate is added to the list of drugs used in the late *influenza* epidemic. Caffrey<sup>187</sup> gave the drug in doses of 10 to 20 grains every four hours the first day, and 5 grains every four hours during the course of the disease. He used it chiefly for its diaphoretic and antifebrile effects. I have commented elsewhere on the various measures used in this disease.

**Radium.** When first introduced as a therapeutic agent the use of radium was largely restricted to superficial growths. The benefits obtained gradually led to its employment in more deeply seated cancerous growths, such as cancer of the uterus and other internal organs. At first the use of the radium in this latter group was restricted largely to the hopeless and inoperable case but its use is being more and more extended in these growths irrespective of the stage. After considerable therapeutic experimenting radium may be said at the present time to occupy a firmly established position.

<sup>184</sup> Indian Medical Gazette, July, 1919.

<sup>185</sup> Journal of the Royal Army Medical Corps, January, 1920.

<sup>186</sup> Lancet, May 22, 1920.

<sup>187</sup> Journal of the American Medical Association, April 24, 1920.

In an article on the late result of radium in the treatment of *cancer of the uterus*, Ransohoff<sup>188</sup> quotes some of the results obtained through operative procedures. Jacobson, in a collection of 5027 cases, found that 1720, or a little over 31 per cent., were operable. In a decade Clark operated on 60 patients and estimated that during that period more than 300 were refused operation, an operability of only 15 per cent. Even more discouraging is the operative mortality which in Jacobson's collection was 18.75 per cent., while Peterson had a previous mortality of 25.4 per cent. Of 1090 cases operated on in Jacobson's series, there were 386 cures, or 35.41 per cent. of patients who were traced, or only 19.32 per cent. of the entire number operated on. Only 11.72 per cent. of the 5027 applying for treatment were cured.

The great difficulty with the surgical treatment of this class of patients is the skill required. In commenting on this aspect of the question, Clark states that: "If an operation or other therapeutic process is to have a permanent place in our armamentarium it must be sufficiently easy to make it available not for a few skilled specialists, but for the great body of surgeons in every quarter of this and other countries."

Ransohoff reports on the late results of 32 cases of malignant disease of the uterus in which radium was used. In this group, 19 per cent. were free from recurrence for from two and a half to five and a half years; 1 patient for five and a half years; 2 patients for over four years; 1 patient for three years and 1 for ten and a half years. Admitting that the series is a small one, the 19 per cent. of cures should be contrasted with the 11 per cent. of cures in Jacobson's statistics, and it should also be borne in mind that there was no fatality. Contrast again the economic saving of work in the hospital, the postoperative suffering and the unbearable sequelæ. Ransohoff is emphatic in the belief that radium treatment should entirely supplant operation not only in the treatment of inoperable cases, but also in the treatment of operable cases of cancer of the cervix. Clark<sup>189</sup> is also of the belief that with a further development in the technic of using radium cancer of the cervix may be removed from the surgical domain. He believes, however, that in cases of cancer of the fundus of the uterus the results obtained by surgery are too satisfactory to be abandoned. In this latter group, radium may be employed if there are complications present which prohibit surgical interference.

Bissell<sup>190</sup> also states the surgical results have been so good in cases of cancer of the fundus of the uterus that all these cases should be submitted to operation. In cancer of the cervix early cases may be operated on and followed by radiation but the latter alone will prove equally efficient.

Recasens<sup>191</sup> states that he has employed radium in the treatment of cancer of the cervix since 1913, and that many cases supposedly

<sup>188</sup> Journal of the American Medical Association, January 17, 1920.

<sup>189</sup> Annals of Surgery, June, 1920.

<sup>190</sup> Minnesota Medicine, June, 1920.

<sup>191</sup> Arch. mens. d'obst. et de gynéc., December, 1919.



inoperable have remained well for three, four and five years. He comments on two unexplainable facts: (1) Why he failed in 30 or 40 per cent. of his over 400 cases when general condition, structure of growth, etc., seemed identical; (2) that sometimes when the radium seemed to have failed completely and the treatment was abandoned as hopeless, the woman returned months later immeasurably improved or even clinically cured. Recasens believes, in the latter instance, that there is a cumulative action from the radium, and the organism had rallied some mysterious forces to its support. He believes that these, as yet unknown, influences must be sought for and made of service.

Another article on the use of radium in the treatment of uterine cancer is contributed by Hansen.<sup>192</sup> He reports 68 cases treated over five years. They were mostly inoperable. About 6 per cent. died from intercurrent disease or have been lost sight of; 27.3 per cent. are known to be living after the five-year interval.

Although but little interested in this question and having no knowledge of the subject aside from what is reported in the literature, I was of the belief that the efficacy of radium in the treatment of cancer of the cervix was widely known to every one. I state this fact because as recently as fifteen months ago the mother of a friend living in a small town in Pennsylvania consulted an eminent surgeon (not a gynecologist) and was told she had an inoperable cancer and that there was nothing to do. No mention was made of radium. About four months ago her discomfort became so marked that she consulted a gynecologist who found an inoperable condition. He recommended radium. Today she is well and free from discomfort of any kind. I mention this simply to call attention to the fact that the extraordinary value of radium is not, as I thought, as well known as it should be.

The most satisfactory results of all from the use of radium are obtained in the treatment of *menorrhagia*, whether due to myoma or fibrosis or to unknown etiology. In this condition, Bissell<sup>193</sup> believes that radiation may be regarded as a specific. Degrais<sup>194</sup> states that the condition producing *menorrhagia* and *metrorrhagia* that are most amenable to treatment by radium are *hemorrhagic metritis* and *fibromata*. Metritis, under which term he groups parenchymatous hemorrhagic metritis and uterine sclerosis, described by Hepp, occurring at any age; however, it is rare in young women, and is most common after forty, especially at the time of the menopause, although it often appears in women who are not menstruating.

In regard to fibromata of the uterus, Degrais asserts that all forms are curable by radium and that a cure can be guaranteed in these cases as certainly as we used to be reserved about promising one.

Degrais gives in detail the technic of his use of radium in these conditions. This, however, need not be considered here.

In using radium in these conditions the immediate results are some-

<sup>192</sup> Ugesk. f. Laeger, March 11, 1920; abstract, Journal of the American Medical Association, May 15, 1920.

<sup>193</sup> Minnesota Medicine, June, 1920.

<sup>194</sup> Canadian Practitioner and Review, March, 1920.

times pain in the kidneys, but more frequently localized pains in the abdomen, and, as in the case of other applications of radium, there may be a feeling of nausea, which seldom produces vomiting, and which ceases with the removal of the radium sound. On the day following treatment, patients show slight lassitude, which is of brief duration.

The time necessary to arrest the hemorrhage is variable. As a general rule, one should not expect it to disappear in the course of a treatment, for often a very free menstrual flow appears after the third application. The patient must be cautioned not to expect too rapid results and to wait for five or six weeks after the last application for the disappearance of all uterine phenomena, whether it be a hemorrhage or an aqueous flow, for the latter often replaces metrorrhagia or menorrhagia for some time after radiation.

As to whether the menses are permanently suppressed by radiation, Degrais says that his experience has shown that women in healthy genital life do not have any permanent cessation of the menses. In 4 cases in which the age of the women treated varied from twenty-five to thirty-five years, the menses disappeared for some months, but reappeared again quite normally. In the treatment of leucorrhea, Curtis<sup>195</sup> used sufficient radium distinctly to influence ovarian activity in these patients. Symptoms of impending amenorrhea in these patients were characterized by greatly increased irregular menstruation, with associated nervousness and tendency to occasional flushes. All returned to symptomatically normal condition within three months.

The process of the arrest of the hemorrhage by uterine radiation is due, primarily, to changes in the mucous membrane; it can also be caused by an action on the ovary, but when this organ is functioning properly it does not sterilize it permanently. This is of importance from the standpoint of an internal secretion and of those troubles which may arise from ovarian atrophy. Degrais states that in addition to the effect on the hemorrhage the patient's general condition improves; ailments due to anemia, dyspepsia, nervousness, etc., disappear.

Aikins<sup>196</sup> also endorses radium as the method of choice in the treatment of uterine fibroids. In uncomplicated cases, no matter how severe, it can be relied upon to arrest the hemorrhage and discharge and cause a shrinkage or complete disappearance of the tumor.

Aikins states that patients treated as long ago as 1905, when radium treatment was in the experimental stage, have remained in good health.

More and more this method is superseding operation in the treatment of fibroids and some form of uterine hemorrhage. The only exceptions to using radium are in cases in which the diagnosis is doubtful, in those in which the fibroids are suppurating, and in those in which the symptoms of pressure render an operation imperative.

Radium, according to Aikins, possesses certain advantages over the  $\alpha$ -rays: (1) The radium can be brought into direct contact with the diseased uterus while the  $\alpha$ -rays depend almost entirely upon their

<sup>195</sup> Journal of the American Medical Association, June 19, 1920.

<sup>196</sup> Canadian Practitioner and Review, September, 1919.



action on the ovaries; (2) in the presence of submucous fibroids associated with endometritis, radium arrests the hemorrhage by a pounding action upon the endometrium and a secondary effect on the ovaries, while with the  $x$ -rays the reverse takes place, and as a result the symptoms of the menopause due to radium are much less than those due to the action of the  $x$ -rays.

In cases which are inoperable owing to the severity of the hemorrhage, radium will often arrest the bleeding and thus render the condition operable.

Graves<sup>197</sup> sounds a warning in regard to the use of radium in cases of uterine hemorrhage. He thinks it is a powerful agent and that there is need for caution in its use. Some of the untoward results are significant chiefly from the psychologic influence which they may exert on the patient, but even these may be of considerable import to the patient's general welfare. The symptoms are nausea, continuation or reappearance of the bleeding, for the cure of which the operation was undertaken, leucorrhea, pain, acute nephritis and nervous symptoms. Employed by those who are properly trained in its use, the warning of Graves would seem to be unnecessary. It does apply to those who are unskilled, and in view of the increasing supply of radium, and its wider distribution, those who use it should have a proper conception of its potency.

In the treatment of *chronic leucorrhea* of cervical origin, Curtis<sup>198</sup> states that it is amenable to cure through dilatation of strictures and treatment with small doses of radium applied at infrequent intervals. The prognosis is less favorable in those cases with chronic cellulitis or uncorrected gross pelvic lesions.

In the treatment of *cancer of the lip*, both in early and advanced cases, Aikins<sup>199</sup> states that the results are equal to or superior to those of surgery. More than 90 per cent. of the early cases have been cured permanently without deformity, and also a fair proportion of the advanced cases. When we compare the 90 per cent. of cures without recurrence with the results of surgery in this condition, the superiority of radium is obvious. Surgical statistics show that the radical operation at an early stage, when there is no apparent involvement of the associated lymph nodes, is followed by recurrence in more than 50 per cent. of cases, and if the lymph nodes are involved at the time of operation, in more than 90 per cent. Radium also has a wide field of usefulness in conditions of the skin and mucous membranes not due to malignancy. It is a valuable method, in Aikins's opinion, for the removal of moles, warts, papillomata, while in the treatment of disfiguring birthmarks, either port-wine stains or angiomata, it is the method of election. It is also of the greatest value in the treatment of keloid, lupus erythematosus and tuberculosis of the skin in its various aspects.

One great advantage of radium over surgery is that it leaves the skin supple, with very little scar formation. Whereas after operation

<sup>197</sup> New York Medical Journal, June 5, 1920.

<sup>198</sup> Journal of the American Medical Association, June 19, 1920.

<sup>199</sup> Canadian Practitioner and Review, September, 1919.



there is a contracted scar, which is frequently the site of recurrence, owing to the irritation to which it is constantly subjected. Aikins has frequently noticed a reappearance of the disease at the site of such wounds.

Thornton<sup>200</sup> also reports remarkable success with radium in dealing with warts, keloids, keratoses, nevi, localized acnoid group (facial), obtrusive scar tissue, moles, sessile indurations, rodent ulcers and epithelioma. Although the treatment may have to be prolonged for months, Thornton states that he has had 100 per cent. perfect results with radium in this group of cases, with the exception of one. The case of failure was an epithelioma of the cheek which had previously been treated with the *x*-rays. He states that radium should never follow the *x*-ray. In this case the growth was aggravated, the malignant process spreading out in all directions.

In the treatment of *goiter*, whether simple or of the exophthalmic type, the *x*-rays often give excellent results. Aikins<sup>201</sup> states that the use of radium in these cases will give, in many instances, results which are nothing less than brilliant. The use of radium in cases of *Graves's disease* slows the pulse-rate, lessens the nervous excitement, causes a variable degree of shrinkage of the gland, and in numerous cases has rendered quite unnecessary a surgical operation.

I have had no experience with radium in these cases but have had excellent results with the *x*-rays. Surgeons are apt to oppose the use of the *x*-ray in the treatment of goiter as they claim it causes numerous and quite dense adhesions about the gland so that removal, if necessary later, is rendered very difficult. In my cases the treatment has been so effective that the question of subsequent operation has never arisen.

The use of the *x*-rays in the treatment of an *enlarged thymus gland* also preceded the employment of radium. Brayton and Henblein<sup>202</sup> state that the treatment of enlarged thymus is simple and specific; it consists solely in radiotherapy. They point out that although for over a decade the *x*-ray had been employed to decrease the size of the gland, the method did not come into general use until about four years ago. Even then the technic of treatment varied so much in the hands of different workers that contradictory reports arose as to its efficacy. The matter was finally clearly defined in 1917 when Friedländer published a series of over 100 cases, in only 4 of which *x*-ray therapy was not successful. Two years ago the writers saw a child in a desperate condition as the result of thymic asthma. The case was so severe that they decided to use radium instead of the *x*-rays in the hope that the radium would act more promptly. The results in their case were so satisfactory that ever since radium has been used exclusively in these cases.

In an experimental *study of the action of radium on bacteria*, Lequeux and Chomé<sup>203</sup> were unable to find that it exerted any destructive effect

<sup>200</sup> Boston Medical and Surgical Journal, September 18, 1919.

<sup>201</sup> Loc. cit.

<sup>202</sup> Boston Medical and Surgical Journal, December 25, 1919.

<sup>203</sup> Arch. mens. d'obstét. et de gynéc., December, 1919.

on the colon and typhoid group, although it arrested the progress of the culture, checked the production of pigment and caused agglutination.

Some bactericidal action was noticeable in the case of the gonococcus and possibly the streptococcus. No effect on the bacteria in the blood stream was demonstrated. They state, however, that one mouse survived a pneumococemia and that rabbits seemed to develop a milder infection after inoculation with staphylococci.

**Rest.** For many years the idea prevailed that climate was the all-powerful influence in treating *tuberculosis*, and even today many laymen and even physicians still cling to this idea. Plenty of fresh air is considered the most important factor in the minds of many. Beginning with the present crusade against tuberculosis some fifteen years ago diet was pushed to the front as its most important thing in the treatment and it is not unusual to hear people say that all that is needed is fresh air and plenty of eggs and milk.

While not denying the value of fresh air and wholesome food, they are of secondary importance to rest in the active stages of the disease and the careful use of exercise later. The value of rest was appreciated by the pioneers in the treatment of the disease, but it has taken years for the importance of this essential principle to sink into the minds of the profession. And even today, after all that has been written on the subject, the necessity of enforcing rest is not appreciated by the majority of physicians. No matter in what part of the body tuberculosis exists, rest for the affected part, insofar as this is possible, is essential. Orthopedic surgeons, for example, have long appreciated the necessity of immobilizing affected joints. Tuberculous lesions of the larynx can often be cured by nothing more than vocal rest plus general hygienic care. Under ordinary conditions it is not possible to completely immobilize the lungs. This, of course, can be done by artificial pneumothorax and when this treatment was first introduced it was believed that it would have a wide application. As a matter of fact, it did not succeed and is rarely used as a routine measure in cases that are considered curable by other methods. The best we can do with the lungs is to minimize their functional activity; this is accomplished, as Schaeffer<sup>204</sup> states, by absolute rest in bed. As he points out, sitting up in bed or a cure chair does not give the complete muscular relaxation needed. The lungs expand least with the patient lying quietly in bed; a little more if sitting up; and still more if the patient is up and about on his feet.

The plan outlined by Schaeffer is that universally followed by phthisiotherapists throughout the world. The patient, when first seen, and no matter how slight the pulmonary lesion or how mild the symptoms, is put to bed for at least a month. In mild cases they can go to the bathroom. But if the temperature fails to fall or the symptoms ameliorate, absolute rest in bed is enforced, namely, the use of a bedpan, bath given by a nurse, etc.; in still more severe and prolonged cases the patient is not allowed to feed himself.



Schaeffer's experience is that of all others in that patients, as a rule, object to going to bed. In the early cases they rarely feel ill and in most instances have been up and about attending to their affairs. For this reason they fail to see the necessity of going to bed. They have never been able to stay in bed, or they will certainly get weak, are several of the numerous of reasons advanced. The doctrine of rest, either complete or limited, is one that the physician finds desirable to inculcate often in a variety of conditions other than tuberculosis. In regard to the latter disease, increased metabolic activity, with resulting wasting, is one of its characteristics. One of the fundamental dicta with regard to metabolism is that it increases with work or muscular effort. Hence the necessity of rest for the active case of tuberculosis in order to minimize, as far as possible, this metabolic activity.

Personally, I have rarely encountered a patient who cannot be convinced as to the necessity of following this advice. One thing is certain, no patient should be allowed to overrule his physician in this respect. Nine-tenths of the success in treating tuberculous patients depends on the patients themselves; the physician can only direct. The patient ill with pneumonia or typhoid fever must have everything done for him and besides he is mentally in no condition to do otherwise. The tuberculous patient, on the other hand, is mentally clear and usually physically capable of being up and about. Those who will not coöperate with the physician usually make unsatisfactory patients and obtain unfavorable results.

Pottenger<sup>205</sup> also has contributed an article on the necessity of rest in treating tuberculosis. Pottenger considers the ideal technic for applying rest and exercise to the treatment of tuberculosis which is followed in the sanatorium. The patient, upon entering the institution, is put to bed. If his maximum daily temperature is near, or only a degree or so above, the normal and there is no other condition to contra-indicate it, he is allowed to get up to wash and go to the toilet and to sit up while his bed is being made. His baths, however, are at first given by the nurse. If toxemia, as indicated by fever, or other contra-indicating conditions are present, then the wash-bowl is brought to the patient while in bed; if severely ill, the urinal and bedpan are used and the bed is made without the patient getting up. Patients are treated with this degree of rest and care until signs of activity lessen and until such a degree of physical and nerve stability has been reached as to warrant the opinion that increased exercise will be beneficial, or at least not harmful.

This long period of rest in his experience is borne well by more than 95 per cent. of patients. The first few days are the most difficult. Lying in bed relieves certain muscles and brings strain upon others. These latter ache, the same as muscles not accustomed to being used in walking ache after a long tramp. This should be explained to the patient. This discomfort disappears in a few days. The patient needs sympathetic encouragement during this first period, and if properly



guided at this time will usually coöperate satisfactorily. This enforced rest and care is, as a rule, a new idea to the patient; it often impresses him with his first idea of the seriousness of his disease, and thus affords him the basis for a whole-hearted necessary coöperation.

How long is the rest treatment to be enforced? So long as the disease is active or symptoms continue annoying. Activity is largely gauged by the presence of fever. Slight afternoon rises in the temperature, up to 99.5°, subside, as a rule, in three or four weeks. The patient is then allowed up for a few hours and this is gradually increased. After two or three weeks, if there is no elevation of the temperature the patient is started on exercise, a few minutes' walking and then gradually increased by two or three minutes daily. The higher the temperature and the longer it takes to reduce it, the longer must the rest treatment be enforced. It may take months. Remember that no measure will reduce fever and that rest must be adhered to indefinitely if necessary. Marked loss in weight, severe cough, nervous exhaustion, etc., call for rest in bed, even with a normal temperature, until these symptoms are controlled.

Why physical energy adversely affects tuberculous patients, either causing or increasing fever in the early stages, or resulting in loss of weight and a relapse in those who have had their disease arrested, is explained by Langworthy and Barott.<sup>206</sup> Light tasks, such as sewing, crocheting or embroidering, call for an average expenditure of about 9 calories an hour more than that of the same person sitting quietly in a chair. Tasks regarded as "harder work" than sewing, such as washing, sweeping or scrubbing, require an increment of at least 50 calories an hour.

Applying this to tuberculous patients, it emphasizes the adverse effect that even slight expenditures of energy exert on the patient with active symptoms, fever, etc. Conversely, complete rest represents the possibility of conserving the energy and minimizing the metabolic activity. Carried still farther it emphasizes the need of cautioning the patients against excessive physical exertion, whether work or athletic activity, after he has recovered from or had his disease arrested.

Of recent years, increasing attention has been given to the case of individuals handicapped by *cardiac disease*. Ida M. Dugan<sup>207</sup> states that from June, 1919, to February, 1920, 305 cardiac patients were referred to the Bureau of the Hospital Social Service Association of New York City. She points out that in finding employment for this class of patients it is necessary to remember that such patients cannot do heavy lifting, cannot climb stairs and cannot operate any but small hand-machines. They are, however, quite well suited for light sedentary work, such as may be found in fountain-pen factories, the jewelry industry, piano factories and the tobacco industry. Women are referred to positions in carding jewelry and in sewing and mending laces. Others are placed in hotels where light work may be found for them.

<sup>206</sup> American Journal of Physiology, June, 1920.

<sup>207</sup> Hospital Social Service Quarterly, May, 1920.

One of the chief difficulties in placing these patients is the fear of employers that such employees would "drop dead" at work. Miss Dugan states that the records of the Bureau show that there have been no sudden deaths among those placed and that no workmen's compensation has had to be paid to any of the persons employed. She thinks that the results obtained are a good indication of what may be accomplished in careful study of the individual case. It is essential that physicians coöperate in such social science work and be prepared to take an active part in it.

Of the 305 patients applying to the Bureau between June, 1919, and February, 1920, 161 were placed in good positions and, at the time of her report, 117 were still in their original positions.

An interesting editorial note<sup>208</sup> on rest as a therapeutic measure quotes a note from Benjamin Disraeli on the subject. The latter writing to a friend who, as has happened to himself, had suffered from a nervous breakdown, said: "Repose is the best medicine for them (nervous breakdowns), and we should guard against the belief that there is any cure for them but a gradual one. Repose, however, is a rare medicine, and impatient suffering is too apt to take refuge in quacks." As the editorial notes: "If all laymen were intelligent—if all could realize that processes of repair in human tissues are not miracles but gradual evolutions in natural processes, which the physician assists and augments—the task of the physician would be less difficult."

Another article on this subject is contributed by St. Lawrence and Adams,<sup>209</sup> who have organized classes of children with cardiac disease. They first attempt to eliminate any item which causes or aggravates the cardiac condition, such as focal infections, undue physical stress, etc. The fitness of each child is then determined for work or exercise. They have divided their cases into three groups: (1) Those with a normal exercise tolerance; (2) those with a lessened tolerance; and (3) those who must be referred for hospital care. The tolerance for work or exercise is built up by strengthening the heart muscle by means of graduated exercises, including calisthenics, climbing stairs and the ordinary forms of games and sports.

**Salicylates.** In a study of the stability of the salicylates, Hanzlik and Wetzel<sup>210</sup> conclude that:

1. Solutions of sodium salicylate gradually deteriorate on standing, the loss being greater with weaker solutions.
2. The destruction is due to some form of living matter such as fungi, since solutions containing a preservative (chloroform), and free from fungi, do not deteriorate.
3. Yeast destroys salicylate, but not nearly as much as the fungus which naturally grows in salicylate solutions.
4. Treatment of salicylate with hashed animal organs results in considerable loss of the drug, which, in part at least, is due to destruction of salicyl. There is no difference between the action of the liver and other organs.

<sup>208</sup> Journal of the American Medical Association, September 4, 1920.

<sup>209</sup> *Ibid.*

<sup>210</sup> Journal of Pharmacy and Experimental Therapeutics, September, 1919.



5. About 20 per cent. of salicylate administered to normal human individuals is destroyed, since the loss cannot be accounted for in sweat and feces or by retention.

6. The destruction in animals (dog and cat) is even greater, amounting to about one-half of the salicylate administered.

7. The destruction of salicylate is markedly increased (about 40 per cent.) in febrile conditions of man, drug habitués (alcohol and morphine), nephritis of both man and dog, and in exophthalmic goiter.

8. The destruction does not appear to be the special function of a given organ such as the liver, since the excretion in certain diseases of the liver in man and in hepatic degeneration in animals was within the normal range.

9. The increased capacity of destruction, therefore, may be ascribed to the general increase in metabolism (catabolism) of febrile conditions and Basedow's disease; to retention with prolonged exposure to the destructive action of the tissues in nephritis.

In a second article, Hanzlik and Wetzel<sup>211</sup> studied the excretion of *salicyl* after the administration of *methyl salicylate* to animals. They found that the excretion of *salicyl* by animals after the administration of *methyl salicylate* is much less (25 per cent.) than after *sodium salicylate* previously reported. After gastric administration the free ester was found in the urine in concentration of 0.2 to 0.52 per cent., and 14.4 per cent. after intramuscular injection. They believe that this may be of importance in explaining the greater analgesic properties and toxicity possessed by *methyl salicylate*, and in urinary and systemic antiseptics.

**Saligenin.** For the purpose of local anesthesia, Hirschfelder, Lundholm and Norrgard<sup>212</sup> found *saligenin* the equal of and less toxic than *procain*, *apothesine* and similar anesthetics. A freshly prepared 12 per cent. solution applied to the mucous membranes of the mouth or nose exerts a definite numbing effect.

**Serum.** In a study of *serum reactions* Péhu and Durand<sup>213</sup> found that the use of a preliminary small dose and then waiting for from one to three hours before giving the main injection protects only against the immediate phenomena, nervous or cardiovascular shock. It does not protect against serotoxic eruption and edema. These are apt to occur after any injection, first or second, and the hypersusceptibility may persist for a long time. As a rule, the serotoxic reactions are harmless.

They state that *adrenalin* in cardiovascular shock is often of great value.

**PNEUMONIA.** The value of serum treatment in lobar pneumonia, providing the type of organism is determined and the proper serum is employed, is attested to by Spooner.<sup>214</sup> The routine advised by Cole was followed by Spooner. In a series of 107 cases due to Type I, the

<sup>211</sup> Journal of Pharmacy and Experimental Therapeutics, September, 1919.

<sup>212</sup> Journal of Pharmacology and Experimental Therapeutics, June, 1920.

<sup>213</sup> Ann. de méd., 1920, No. 3, 7.

<sup>214</sup> Boston Medical and Surgical Journal, February 26, 1920,



mortality was reduced to 7.5 per cent. (Cole). In the series at Camp Devens during the influenza epidemic, the mortality of such cases treated with a high titre serum was reduced from 43 to 7 per cent. Spooner concludes that 30 per cent. of cases of acute lobar pneumonia are due to Type I organism, and that an immediate diagnosis of the type of organism is essential for the early administration of the appropriate serum. The use of polyvalent sera is irrational and unjustified. The careful use of Type I serum for Type I pneumonia is safe. It has reduced the spread of the disease process and the mortality to a sufficient extent to indicate its universal application.

Although a very large number of reports on the use of sera of various sorts followed the recent influenza epidemic, opinions varied greatly as to the results. The only serum which really stood the test is the Type I. In other words, the first essential in these cases is to determine the type of the infecting pneumococcus and if it proves to be Type I the specific serums for that type should be used.

DYSENTERY. The use of antidyenteric serum in the treatment of bacillary dysentery depends for success on its early employment. Klein<sup>215</sup> divides dysentery into three stages: (1) The first stage extends from the onset of the illness to a period somewhere about the fifth or sixth day. It is in this period that the serum has a most favorable effect, both as regards averting a fatal result and hastening recovery. A minority of cases fail to respond to their early treatment. (2) In the intermediate stage, extending from about the sixth to the tenth day, the patient dies or recovers irrespective of serum treatment. But the rate of completeness of recovery may still be affected by serum, especially if given in large doses (such as 100 c.c.). (3) In the last stage, that of dehydration and profound intoxication, starting about the tenth day, serum treatment is useless. A minority of cases which have lasted to the tenth day or beyond it (without passing into the third stage) are still benefited by serum given in sufficient amount.

Klein states that the serum should be given in large doses, from 60 to 100 c.c., and is best given intravenously. To obtain satisfactory results, the serum must be employed early in the disease.

EPIDEMIC CEREBROSPINAL MENINGITIS. In treating this disease with serum introduced into the spinal canal, Sailer<sup>216</sup> states that it is desirable to remove as much of the spinal fluid before introducing the serum as possible. In conscious patients the flow of the fluid is increased by having the patient count to 100. The serum is introduced by means of a Lohé syringe. The injection should be made very slowly, from 1 to 2 c.c. per minute. This is easily estimated if the syringe barrel is graduated. The entire operation usually requires about half an hour. The amount of serum injected should be about 10 c.c. less than the amount of fluid withdrawn. If this rule is observed, Sailer states that no symptoms of pressure other than perhaps a very slight transient headache will ever be produced. As soon as the serum has been introduced, the tube should be removed from the end of the

<sup>215</sup> Journal of the Royal Army Medical Corps, October, 1919.

<sup>216</sup> Pennsylvania Medical Journal, February, 1920.

needle, the stylet placed into it and the needle slowly withdrawn. A drop of iodine is placed over the site of the puncture and no further dressing is required.

The only danger in the use of the serum, providing it is a good serum, is *anaphylaxis*. The ordinary desensitizing dose of 1 c.c. injected subcutaneously one hour before puncture is made has proved to be an adequate precaution. If there is evidence of anaphylaxis, such as the appearance of a swelling, it is desirable to give a few more subcutaneous doses, increasing in size at intervals of one hour. As a general rule, Sailer states that anaphylactic shock from intrathecal administration of serum, even in susceptible individuals, is far less severe than it is when intravenous administration is employed.

Another danger of serum therapy is to mistake an attack of serum sickness for a recurrence of the disease. If at this time serum is injected, a severe anaphylactic shock usually ensues. The distinction between serum sickness and a recurrence of the meningitis is not always easy. The serum sickness occurs about six days after the last injection and during the attack of serum sickness the spinal fluid contains sugar, while during the course of the meningitis sugar is almost always absent.

If symptoms pointing to a general meningococcic sepsis are present, the serum may be given intravenously. If given by this route, the same technic is employed as in the case of antipneumonic serum. The serum should be injected very slowly, at the rate of 1 c.c. per minute until 15 c.c. are given; if there are no untoward manifestations, the remainder may be injected more rapidly. Herrick recommends from 50 to 100 c.c. two or three times in the first twenty-four hours.

**Silver.** The use of a silver nitrate solution for colonic irrigations is reported on favorably by Thompson<sup>217</sup> in cases of *amebic dysentery* which have resisted emetine and other drugs commonly used in this condition. He employed silver nitrate 1 dram in 1 ounce of water and this was added to 2 pints of warm water and given as a high irrigation; it is retained for about ten minutes in each case in which he employed the irrigations. There was marked improvement after the second or third day. The pain in the left iliac fossa is relieved and also the constant desire for and straining at stools.

I have used irrigations of silver nitrate with benefit for some years. Only recently a young woman with advanced pulmonary tuberculosis was relieved of a troublesome *diarrhea* by high injections of this solution. In many tuberculous patients the diarrhea is due to a chronic catarrhal colitis, with or without tuberculous ulcers, and I have found nothing more satisfactory than a weak solution of silver nitrate.

Agar<sup>218</sup> reports favorably on the treatment of *hay fever* by means of the local application of silver nitrate (30 grains to the ounce). He applies this solution thoroughly to the vestibule of the nose, paying particular attention to two spots, the first is high up on the outer wall, and the second is the floor, from  $\frac{1}{2}$  to  $\frac{3}{4}$  inch back from the orifice. No part of the vestibule must be missed, and the nostril must be

<sup>217</sup> Journal of the Royal Army Medical Corps, May, 1920.

<sup>218</sup> British Medical Journal, July 24, 1920.



stretched to open up the folds. No application is made to the mucous membrane. All patients with *nasal rhinorrhea* have been cured by this method. Some cases of *asthma* have also responded favorably.

It is well to remember in administering silver nitrate internally that the drug cannot be given indefinitely without the danger of producing *argyria*. This condition is much less common than formerly when silver nitrate was so generally employed in the treatment of gastric ulcers. Prescriptions for this drug should only be filled on a physician's order. Guillemot, Michaux and Duval<sup>219</sup> report a case of *argyria* in a case of *tabes* to which silver nitrate had been administered daily for ten years.

**Sodium Bicarbonate.** The term *acidosis* is applied to that condition of *diabetic coma* which is chiefly due to the breaking down of the fats and to the starvation of the patient of carbohydrates. The condition is characterized by breathing which is rapid and deep and at times may simulate the Cheyne-Stokes type. The condition is not associated with cyanosis and the lips of the patient may appear more pink than normal. It is not due to an interference with the oxygen-carrying forms of the blood, but arises because the body has been deprived of its carbonates and other bases, to such an extent that the  $\text{CO}_2$  is not carried to the lungs by the blood stream as it is in health.

As Hare<sup>220</sup> points out, it is well to remember that the blood stream is not more acid than normal but there is, in acidosis, an excess of beta-oxybutyric acid in the body which acts as a toxic substance. This can only be gotten rid of by being oxidized into diacetic acid, and then one step further, into non-toxic acetone. Hare states that the use of bicarbonate of sodium, by means of the Murphy drip, by hypodermoclysis, or even by intravenous injection, does good, not as an antacid, but because it provides the patient with the carbonates of which the system has been robbed, and by so providing carbonate the  $\text{CO}_2$  is carried to the lungs and eliminated and oxygen can then be utilized by the tissues to reduce the toxic substance. Hare recommends, in diabetic acidosis, the Murphy drip, with or without the bicarbonate, glucose, levulose or, what he frequently employs, dextrimaltose. He gives a solution of 5 per cent. bicarbonate of sodium and 5 per cent. of dextrimaltose. In urgent cases this may be given intravenously.

In addition to diabetes, acidosis may occur in a number of other conditions. Gittings<sup>221</sup> has contributed an article on the occurrence of acidosis in early life associated with gastro-intestinal conditions. In treating these conditions, the maintenance or replenishment of the water in the tissues and supplying alkali to prevent or overcome alkali depletion are the most important factors. The need for water is emphasized by the dry, putty-like skin and subcutaneous tissues which the patients of the diarrheal type so often show. If acidosis is suspected, the urine should be tested for acetone and diacetic acid,

<sup>219</sup> Bull. médicale, July 17, 1920.

<sup>220</sup> Therapeutic Gazette, 1920, p. 542.

<sup>221</sup> Ibid., July 1, 1920.



and the tolerance to sodium bicarbonate determined. If the latter shows definite increase of tolerance (uric acid after 2 or 3 grams of sodium bicarbonate), the administration of soda by mouth or rectum is justified. In severe cases, it may be given intravenously.

The preparation of the sodium solution is of great importance as it cannot be sterilized by heat without drawing off carbon dioxide and reducing the bicarbonate to carbonate. The latter is too irritating to be used safely. As the sodium bicarbonate in bulk is always sterile, a 4 per cent. solution can be made with freshly sterilized (cooled) water and sodium bicarbonate, chemically pure, from a freshly opened bottle. A rigid aseptic technic must be observed.

In children, if it is necessary to introduce the solution into the blood stream, the longitudinal sinus offers the easiest route.

In severe cases of diarrhea, the sodium bicarbonate may be used as a preventive in doses of 5 to 10 grains by mouth every three hours combined with bismuth subcarbonate.

Gittings states that the object of the use of soda must not be forgotten, namely, to replenish the carbonates of the blood and tissues. Success in treatment is indicated by: (1) Change in reaction of urine from acid to alkaline; (2) restoration of the normal bicarbonate reserve of the plasma (Van Slyke's method); (3) restoration of normal  $\text{CO}_2$  tension in the alveolar air (Marriott's method); (4) restoration of the normal reaction of the blood serum to phenolphthalein (Sellard's method).

**Sodium Nitrite.** Poisoning with this drug is not common, as its use commercially is limited. Oliver,<sup>222</sup> in reporting a case of accidental poisoning, has reviewed the literature on the subject. He quotes a report of Barth who noted poisoning in cattle due to the presence of sodium nitrite (in fertilizer) in their fodder. The toxic manifestation in animals is practically identical with those occurring in man. The symptoms are as follows:

(1) Drowsiness and giddiness; (2) primary elevation of temperature, followed by a secondary fall; (3) fibrillar contractions of the muscles; (4) deep, labored respirations; (5) vomiting and yawning (in dogs); (6) browning of the color of the blood (due to the formation of methemoglobin); (7) occasional paralyses; (8) death without spasm or convulsion; (9) accompanying the above, of course, there occurs a marked fall in blood-pressure.

Cases of chronic poisoning have been noted among aniline workers, the chief symptom noted being headache, cyanosis, low blood-pressure, hemoglobinuria and a rather severe secondary anemia. A few cases of poisoning have been reported following the therapeutic use of the drug.

The case reported by Oliver was that of a man who found what he supposed was a jar of salt. He ate six or eight radishes which he dipped into the salt. In ten or fifteen minutes he felt dizzy and it was noticed that his face began to "color up." He was taken to a hospital comatose, dyspneic, cyanotic and with the skin bathed in a profuse, cold perspi-

ration. There were spasmodic twitchings of the arms and hands and convulsive contraction of the jaws. During these attacks he crunched his teeth, and it was impossible to separate his jaws. The breathing was stertorous and irregular with periods of apnea lasting from fifteen to twenty seconds and followed by irregular, violent, noisy and forceful respirations. The pulse was large, dicrotic, regular. The blood-pressure was systolic 98, and diastolic 60. No other abnormal physical findings were detected.

He was given an intravenous injection of Fischer's solution (500 c.c.), and inhalation of oxygen. The following day the symptoms had nearly disappeared and he made an uneventful recovery.

**Strophanthin.** The imperative need of obtaining physiological effects from the digitalis group is readily seen. Inasmuch as some member of this group is invariably employed in serious cardiac conditions, the need of purity on the part of the drug is great. Having observed wide variation of potency in the biologic assays of several lots of a commercial preparation of ouabain (g-strophanthin) furnished in ampoules, Levy and Cullen<sup>223</sup> investigated the cause. They found that the sterilized solutions were decidedly alkaline in reaction, whereas freshly prepared aqueous solutions of the drug were neutral or slightly acid. The drug is readily made inert by heating with alkalis. They found that the ordinary soft glass usually employed in making the ampoules for the sterile solutions yielded sufficient alkali in heating, to change the reaction of the distilled water and thus render the strophanthin inert. They state that the difficulty may be averted by using containers made of hard glass.

Roderburg<sup>224</sup> states that he has treated about 100 patients with strophanthin in the last eight years. He has not found the intravenous injections dangerous, even with very high blood-pressure and in the final stages of chronic nephritis. In fact, he states that severe cardiac insufficiency associated with nephritis is more liable to be influenced by the intravenous use of strophanthin. As an initial dose he recommends not more than 0.5 mg. and often does not use more than 0.3 or 0.4 mg. The maximum dose is from 0.75 to 1.0 mg. The interval between doses should be twenty-four hours at least and usually from two to five days.

He thinks the drug especially indicated in cases of mild cardiac insufficiency.

Certain cases of dropsy of non-renal origin are not influenced by strophanthin and yield only to *theobromin* preparations.

**Sulphuric Acid.** The value of dilute sulphuric acid in the treatment of *staphylococcus* infection is reiterated by Reynolds.<sup>225</sup> Since 1915, when he first directed attention to this subject, he has had a number of patients who were cured by sulphuric acid when vaccines and other measures had failed. In an inveterate case of *acne* which had resisted every method of treatment, he achieved a complete cure

<sup>223</sup> Journal of Experimental Medicine, March, 1920.

<sup>224</sup> München. med. Wehnschr., February 6, 1920.

<sup>225</sup> Lancet, March 13, 1920.

in three weeks. In this case the whole body was covered with acne pustules. This patient was given 30-minim doses of dilute sulphuric acid (made by adding 3 fluidounces of strong acid to 29 fluidounces of water). Small doses are ineffective. To obtain results the acid must be given in from 20- to 30-minim doses, diluted with a wineglassful of water.

**Tyramin.** According to Barbour and Maurer,<sup>226</sup> tyramin is the superior of all other drugs, such as caffein, atropin, etc., to overcome morphin depression.

**Vaccines.** In an editorial article<sup>227</sup> the limitations of vaccine treatment are pointed out. Autogenous vaccines seem to have been useful in cases of furunculosis and localized abscesses in soft tissues; in acne vulgaris, in pyelitis and cystitis due to the colon bacillus and chronic bronchitis.

Vaccines have not given good results in infection of bone or infections in cavities with rigid walls, infection of the intestinal tract and infection of the uterus and adnexa.

As Theobald Smith emphasized several years ago, vaccines are not to be employed in the acute stages of an infectious process and are therefore contra-indicated in septicemia and pyemia in the acute stages; in malignant endocarditis; and in acute infectious diseases in general.

**BRONCHIAL ASTHMA.** The treatment of this disease by means of protein substances or vaccines has attracted a great deal of attention during the past few years. Much credit is due to Walker and his co-workers at the Brigham Hospital for their researches on this subject. It is now generally recognized that a large group, if not all cases of bronchial asthma, are due to a protein poison. In some cases this is quickly determined; in others, a most painstaking search is needed. The commonest form is that due to the inhalation of horse dandruff or the pollen of flowers or weeds. It is becoming more and more apparent, however, that not a few cases are caused by the digestion of a protein, such as eggs. In still another group the protein hypersensitiveness is caused by bacteria.

Walker<sup>228</sup> reports on 28 cases of bronchial asthma treated with vaccines of the bacteria to which they were sensitive; 75 per cent. were relieved of asthma and 21 per cent. were improved. The majority of these cases were given autogenous vaccines composed of the *Staphylococcus pyogenes aureus*, *streptococcus* or diphtheroids. In this connection it might be mentioned that there are a very considerable number of cases which are called asthma but which do not have the characteristic paroxysmal attacks of expiratory dyspnea. As a rule, they are middle aged or older, suffer from chronic bronchitis, which is usually somewhat better in summer and are subject to varying degrees of dyspnea. The dyspnea is usually aggravated if they catch a fresh cold. Walker has distinguished this group as asthmatic chronic bronchitis. Autogenous vaccines are often very helpful in these cases.

<sup>226</sup> Journal of Pharmacology and Experimental Therapeutics, June, 1920.

<sup>227</sup> Journal of Laboratory and Clinical Medicine, May, 1920.

<sup>228</sup> Archives of Internal Medicine, February, 1919.



The prevailing organisms in the cases for which I have had vaccines made are staphylococci, streptococci (non-hemolytic) and diphtheroid organisms. In determining the protein which is the cause of the asthma or hay fever, it is usual to make skin tests with a number of the commoner proteins. It is well to remember that more than one protein may be at fault and it is quite likely that failure sometimes occurs because the vaccine contains but one of the offending substances. Having determined the protein to which the patient is sensitive, a vaccine is then given. In the case of hay fever, the immunization should be commenced several months prior to the expected attack.

Sanford,<sup>229</sup> in a preliminary report from the Mayo Clinic, states that tests made on more than 800 patients showed that more than 500 were entirely negative in their skin reaction; the reactions in 100 more were doubtful. The remainder, about 200, had definite skin reactions. The greatest number of reactions were caused by proteins derived from foods, the greatest number being due to egg-white (11 in all); 28 were sensitive to vegetable proteins; 25 to grain; and 28 to some of the animal emanations, horse dander being the commonest. Fruits, apparently, have little to do with asthma, although in several instances the banana was a definite factor. Of patients sensitive to ragweed and other autumn pollens, 52 were definitely positive. Of 365 tests made to determine sensitiveness to staphylococci, all were negative.

The use of vaccines in the treatment of bronchial asthma and hay fever is favorably reported on by Hutcheson and Budd.<sup>230</sup> In 53 cases (74.6 per cent. of cases treated) they obtained complete relief or a definite decrease in the frequency of the attacks.

Gottlieb<sup>231</sup> states that the treatment of bronchial asthmatics who are sensitive to epidermal proteins is very satisfactory, and it is in this class of cases that we procure our most striking results. Patients suffering from anaphylaxis due to cat hair, dog hair, feathers, etc., or patients exposed to animal emanations, such as furriers, cattle dealers or stablemen, can, as a rule, be readily relieved.

**DIPHTHERIA.** It is well known that it is often a most difficult thing to get rid of the Klebs-Loeffler organism following an attack of diphtheria. As a result, patients sometimes are held in quarantine for weeks owing to the persistence of the bacilli in the throat. Nearly every year there are one or more articles on the value of some agent to relieve this condition. Brownlie<sup>232</sup> reports most favorably on the use of a diphtheria vaccine. He states that antiseptic throat applications are unreliable cures for the carrier and the positive convalescent throat. By using diphtheria vaccine there is produced a well-defined degeneracy in the morphological appearance of the cultured organism, followed by its complete dispersal from the locality invaded. He concludes that diphtheric vaccine is effective in the treatment of the positive throat

<sup>229</sup> Minnesota Medicine, April 20, 1920.

<sup>230</sup> Virginia Medical Monthly, February, 1920.

<sup>231</sup> Journal of the American Medical Association, April 3, 1920.

<sup>232</sup> Lancet, March 27, 1920.

of diphtheria convalescents, and its use is administratively and economically sound.

**WHOOPING-COUGH.** Luzzatti<sup>233</sup> is favorably impressed with anti-pertussis vaccine as a prophylactic. He employed it in three families with numerous children when one of the children had developed the disease. No attempt was made to isolate the children and in no case did the disease occur.

**TYPHOID FEVER.** Sir Almroth Wright states that the fact that the natural resistance to typhoid fever can be powerfully reënforced by inoculation with typhoid vaccine is one of the great facts the War added to our knowledge of immunization. As a matter of fact, this fact was amply demonstrated by the results obtained in the American Army before the Great War ever started. The removal of typhoid fever as one of the great menaces to military forces is one of the triumphs of modern preventive medicine. Thus, Victor C. Vaughn, Jr.,<sup>234</sup> points to the fact that the incidence of the typhoid group of diseases in the American Expeditionary Forces was *less than 0.1 per cent. as compared with 20 per cent. for the Spanish-American War*. In a study of 270 cases of typhoid fever occurring in vaccinated individuals, Vaughn states that the clinical picture was similar to that occurring in the unvaccinated.

In an experimental and clinical study of the effect of antityphoid vaccination on pregnancy, Guérin-Valmale and Vayssière<sup>235</sup> found that the pregnancy progresses the same in the vaccinated as in the non-vaccinated, and the fetus shows no injurious influence from the vaccine even in the last half of the pregnancy. The fetal serum also acquires agglutinating power.

**X-rays.** The knowledge of the great value of the x-rays in the treatment of *uterine fibroids* has become quite general. A number of favorable reports have appeared during the past year. Bécclère<sup>236</sup> reports a series of 500 cases. In 84.5 per cent. of his cases the fibromas projected into the abdomen from 1 to 30 cm. above the pubis. They began to subside in size even after the second or third treatment, shrinking about 1 cm. a week; menstruation usually was not arrested under two or three months. In 60 per cent. of the cases only from twelve to fourteen treatments were necessary, so that the course took only ten or twelve weeks. During this time the women continued their usual life and there was no suffering of any kind. Belot<sup>237</sup> credits Foveau de Courmelles with being the pioneer in this method of treatment, his results being published in January, 1904. Belot states that from 95 to 96 per cent. of cures can be expected from the use of the roentgen rays. There is no evidence that this treatment will transform a fibroma into a cancer, while on the other hand there is an accumulating evidence that radiotherapy may cure cancer of the uterus.

<sup>233</sup> Policlinico, April 12, 1920; abstract, Journal of the American Medical Association, July 3, 1920.

<sup>234</sup> Journal of the American Medical Association, April 17 and 24, 1920.

<sup>235</sup> Gynécologie et Obstétrique, 1920, No. 3, 1.

<sup>236</sup> Arch. mens. d'obst. et de gynec., August, 1919; Journal de Radiologie et d'électrologie, November, 1919.

<sup>237</sup> Bull. médicale, June 26, 1920.



He quotes Delbet to the effect that: "The fibroma fleeing from the knife, melts away under the rays from the roentgen tube."

Cauchoux,<sup>238</sup> in a general review of the use of the  $x$ -rays in fibromas cites 3 cases reported by Ménard in which conception followed the use of the  $x$ -rays, showing that exposure of the ovaries to the rays does not necessarily prevent pregnancy later. Contrary to Belot's statement Cauchoux thinks that beginning necrosis or malignant degeneration may be stimulated by the use of the rays.

Gagey<sup>239</sup> believes that *radium* is the superior agent for the treatment of small fibromas, not larger than the ovum of a three or four months' pregnancy.

In reporting 49 cases of uterine myomas subjected to roentgen-ray treatment, Boije<sup>240</sup> states that hemorrhage ceased entirely in 83.7 per cent. and the tumors shrivelled in 95.5 per cent. He does not believe that degenerated or gangrenous myomas are adapted for radiotherapy. Also that operative interference will not act more quickly and more certainly on pain although it may be wise to reduce the hemorrhagic tendency with radiotherapy and wait for the anemia to improve before attempting the operation. Boije believes that conservative enucleation should be the rule before the age of forty or forty-two.

The essential thing for the general practitioner to remember is that the use of radium or the  $x$ -rays is highly successful in the treatment of these tumors and, unless the specialist rules otherwise, should be made available for patients so affected.

ENLARGED THYMUS. I have commented elsewhere (see Radium) on the excellent results obtained in hyperplasia of the thymus by means of radium. Brooks<sup>241</sup> believes that the  $x$ -rays furnish the best method of treating this condition. He states that he has seen improvement in the most alarming cases take place in from eighteen to forty-eight hours, with sometimes almost total abatement of symptoms which have existed for months.

The successful use of the roentgen rays in a case of *polycythemia* is reported by Forschbach.<sup>242</sup> The long bones were treated with deep irradiations. In Forschbach's opinion, the case is chiefly remarkable because of the exceptionally long duration of the treatment. Treatment was begun in 1916, and two courses of eight days given. The treatment was then abandoned. Treatments were resumed in September, 1917, and continued until April, 1919. The highest red cell count in this case was 12,500,000; this fell under treatment to 7,796,000 and the hemoglobin to 90 per cent. He states that the fall in the white cells must be as carefully watched as that of the red cells in order to avoid serious leukopenia.

Marked improvement in a case of *acromegaly* from the use of the  $x$ -rays is reported by Webster.<sup>243</sup> After being improved remarkably,

<sup>238</sup> Bull. médicale, June 26, 1920.

<sup>239</sup> Ibid.

<sup>240</sup> Friska Läkarsällskapets Handlinger, January, 1920; abstract, Journal of the American Medical Association, May 15, 1920.

<sup>241</sup> Ohio State Medical Journal, January, 1920.

<sup>242</sup> Berliner klin. Wchnsch., November 3, 1919.

<sup>243</sup> Archives of Radiology and Electrotherapy, January, 1920.



so far as annoying symptoms were concerned, the patient was lost sight of for ten years; in the meantime her condition had become aggravated.

**Yeast.** The use of yeast in the treatment of *arthritis deformans* is suggested by Spencer.<sup>244</sup> He was led to try this accidentally. A case of severe arthritis deformans under his care had been treated with a variety of drugs but without avail. A yeast cake was given thrice daily after meals for a laxative effect. It was noted shortly after this that the arthritic condition began to improve. The patient, a boy, aged seventeen years, was finally changed from an invalid to a self-supporting member of society. Three other patients, older individuals, suffering from a milder form of arthritis deformans were decidedly improved by the yeast treatment. Spencer feels that the improvement noted in these cases warrants a further trial of the yeast in order to determine its value.

The use of yeast as a food has been studied by Hawk, Smith and Holder.<sup>245</sup> In using the yeast for this purpose, they substitute it for only a portion of the proteins, 9 to 29 per cent. The yeast may be dried, baked or boiled, so as to kill its enzyme, without materially modifying its nutritional properties. It may be given stirred up in milk, or orange-juice, baked in bread or any other convenient method. In a study of the metabolism of six men, they found that four of the six showed an improved nitrogen balance when left on yeast diet, and, further, that this yeast diet produced an average daily gain of about 0.4 gram of nitrogen per man above that noted before yeast was fed. They feel that this shows that these men found yeast a satisfactory article of diet. They even go so far as to claim that they have demonstrated that the nitrogen of yeast is preferred by the nutritional mechanism of certain individuals to the nitrogen in the form of such staple foods as wheat.

<sup>244</sup> Therapeutic Gazette, May, 1920.

<sup>245</sup> American Journal of Physiology, 1919.

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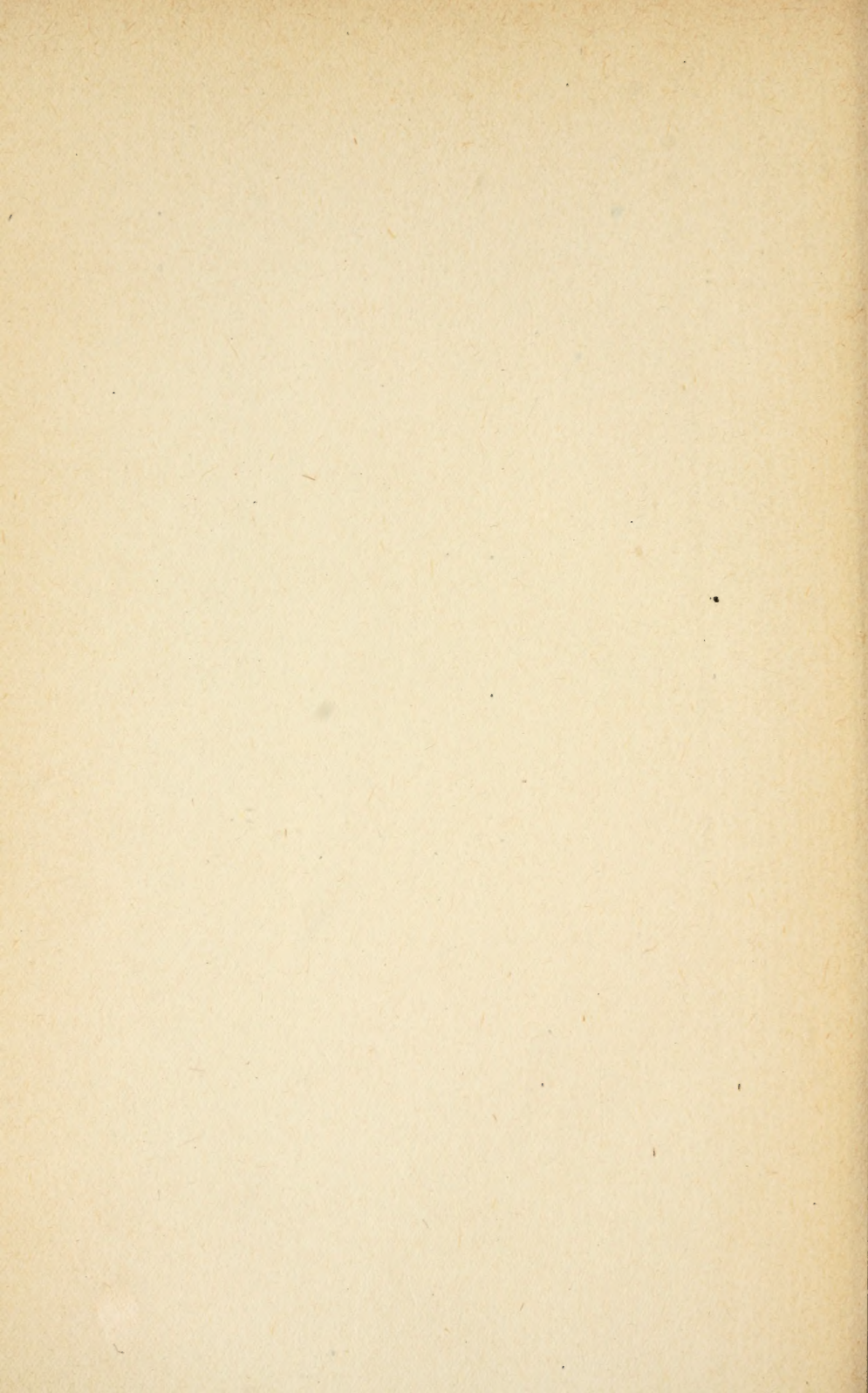
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